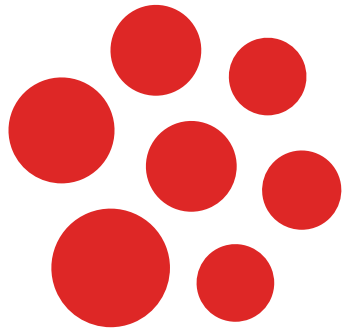


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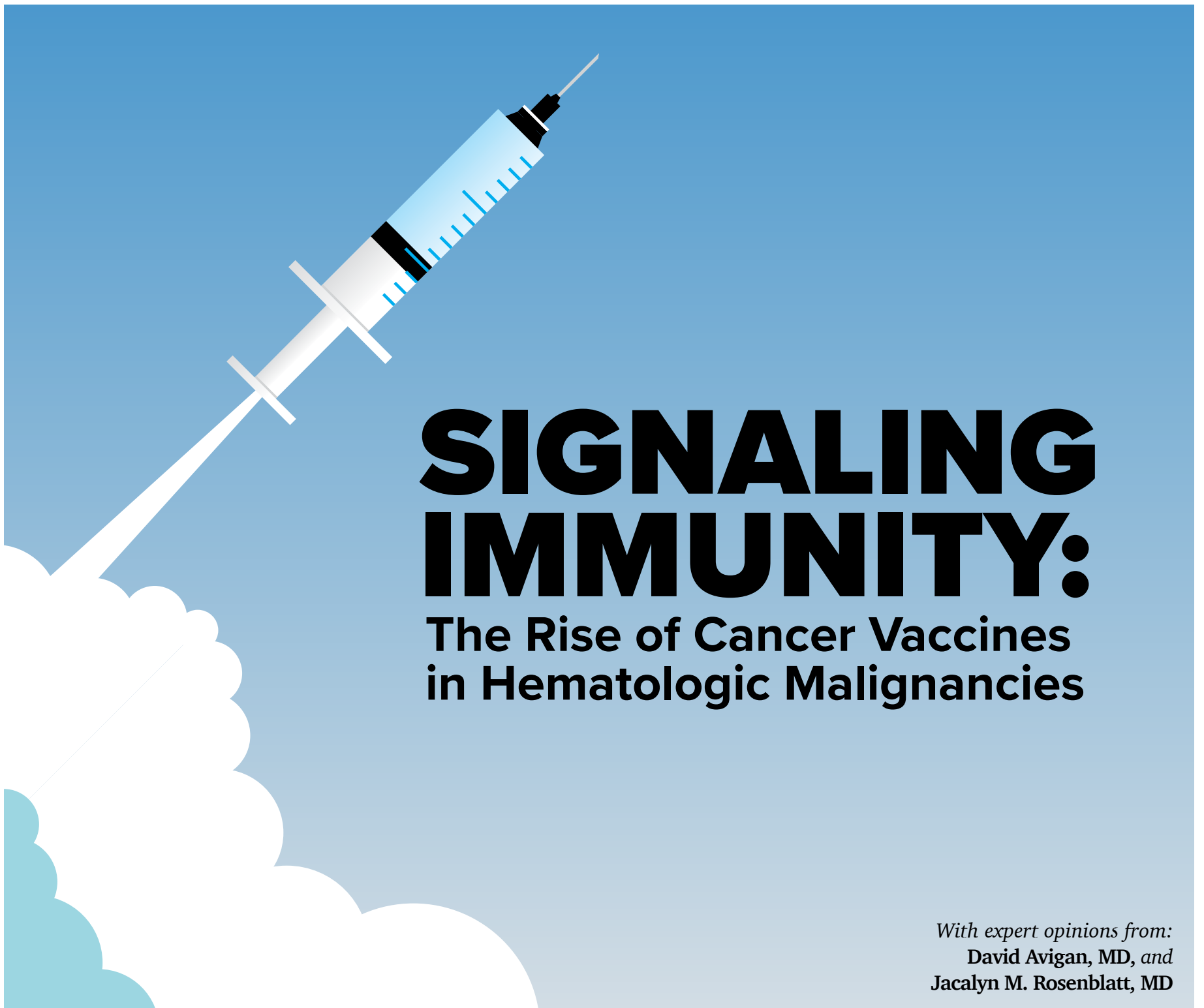
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SIGNALING IMMUNITY:

The Rise of Cancer Vaccines in Hematologic Malignancies

*With expert opinions from:
David Avigan, MD, and
Jacalyn M. Rosenblatt, MD*

MAIL TO:



KIMBERLY KU, MD
Empathy: A Hard Science
for Better Communication
and Research

OJJAARA for myelofibrosis (MF)
with anemia

Ojjaara
(momelotinib)
200 mg - 150 mg - 100 mg tablets

Multifaceted disease management starts here

Take on multiple aspects of myelofibrosis

Start with OJJAARA—The first & only FDA-approved JAK inhibitor indicated specifically for patients who have myelofibrosis with anemia.^{1,2}

OJJAARA was assessed for:

- Total Symptom Score Reduction
- Spleen Volume Reduction
- Transfusion Independence



Explore the data
in JAKi-naïve and
JAKi-experienced
patients



Not an actual patient.

FDA=US Food and Drug Administration;
JAK=Janus kinase.

INDICATION

OJJAARA is indicated for the treatment of intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF [post-polycythemia vera (PV) and post-essential thrombocythemia (ET)], in adults with anemia.

IMPORTANT SAFETY INFORMATION

Risk of Infections

- Serious (including fatal) infections (e.g., bacterial and viral, including COVID-19) occurred in 13% of patients treated with OJJAARA. Infections regardless of grade occurred in 38% of patients. Delay starting therapy until active infections have resolved. Monitor patients for signs and symptoms of infection and initiate appropriate treatment promptly.

Hepatitis B Reactivation

- Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine transaminase (ALT) or aspartate transaminase (AST), have been reported in patients with chronic hepatitis B virus (HBV) infection taking

Janus Kinase (JAK) inhibitors, including OJJAARA. The effect of OJJAARA on viral replication in patients with chronic HBV infection is unknown. In patients with HBV infections, check hepatitis B serologies prior to starting OJJAARA. If HBsAg and/or anti-HBc antibody is positive, consider consultation with a hepatologist regarding monitoring for reactivation versus prophylactic hepatitis B therapy. Patients with chronic HBV infection who receive OJJAARA should have their chronic HBV infection treated and monitored according to clinical HBV guidelines.

Thrombocytopenia and Neutropenia

- New or worsening thrombocytopenia, with platelet count less than $50 \times 10^9/L$, was observed in 20% of patients treated with OJJAARA. Eight percent of patients had baseline platelet counts less than $50 \times 10^9/L$.

Please see additional Important Safety Information on the following page with accompanying Brief Summary of the full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont'd)

Thrombocytopenia and Neutropenia (cont'd)

- Severe neutropenia, absolute neutrophil count (ANC) less than $0.5 \times 10^9/L$, was observed in 2% of patients treated with OJJAARA.
- Assess complete blood counts (CBC), including platelet and neutrophil counts, before initiating treatment and periodically during treatment as clinically indicated. Interrupt dosing or reduce the dose for thrombocytopenia or neutropenia.

Hepatotoxicity

- Two of the 993 patients with MF who received at least one dose of OJJAARA in clinical trials experienced reversible drug-induced liver injury. Overall, new or worsening elevations of ALT and AST (all grades) occurred in 23% and 24%, respectively, of patients treated with OJJAARA; Grade 3 and 4 transaminase elevations occurred in 1% and 0.5% of patients, respectively. New or worsening elevations of total bilirubin occurred in 16% of patients treated with OJJAARA. All total bilirubin elevations were Grades 1-2. The median time to onset of any grade transaminase elevation was 2 months, with 75% of cases occurring within 4 months.
- Delay starting therapy in patients presenting with uncontrolled acute and chronic liver disease until apparent causes have been investigated and treated as clinically indicated. When initiating OJJAARA, refer to dosing in patients with hepatic impairment.
- Monitor liver tests at baseline, every month for 6 months during treatment, then periodically as clinically indicated. If increases in ALT, AST or bilirubin related to treatment are suspected, modify OJJAARA dosage based upon Table 1 within the Prescribing Information.

Severe Cutaneous Adverse Reactions (SCARs)

- Severe cutaneous adverse reactions (SCARs), including toxic epidermal necrolysis (TEN), have been observed in some patients treated with OJJAARA.
- If signs or symptoms of SCARs occur, interrupt OJJAARA until the etiology of the reaction has been determined. Consider early consultation with a dermatologist for evaluation and management.
- If etiology is considered to be associated with OJJAARA, permanently discontinue OJJAARA and do not reintroduce OJJAARA in patients who have experienced SCARs or other life-threatening cutaneous reactions during treatment with OJJAARA.

Major Adverse Cardiovascular Events (MACE)

- Another JAK inhibitor increased the risk of MACE, including cardiovascular death, myocardial infarction, and stroke [compared with those treated with tumor necrosis factor (TNF) blockers] in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated.
- Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OJJAARA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Inform patients receiving OJJAARA of the symptoms of serious cardiovascular events and the steps to take if they occur.

Thrombosis

- Another JAK inhibitor increased the risk of thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis (compared with those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated. Evaluate patients with symptoms of thrombosis and treat appropriately.

Malignancies

- Another JAK inhibitor increased the risk of lymphoma and other malignancies excluding nonmelanoma skin cancer (NMSC) (compared with those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated. Current or past smokers were at increased risk.
- Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OJJAARA, particularly in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers.

Adverse Reactions

- The most common adverse reactions ($\geq 20\%$ in either study) are thrombocytopenia, hemorrhage, bacterial infection, fatigue, dizziness, diarrhea, and nausea.

Organic Anion Transporting Polypeptide (OATP)1B1/B3 Inhibitors

- Momelotinib is an OATP1B1/B3 substrate. Concomitant use with an OATP1B1/B3 inhibitor increases momelotinib maximal concentrations (C_{max}) and area under the concentration-time curve (AUC), which may increase the risk of adverse reactions with OJJAARA. Monitor patients concomitantly receiving an OATP1B1/B3 inhibitor for adverse reactions and consider OJJAARA dose modifications.

Breast Cancer Resistance Protein (BCRP) Substrates

- Momelotinib is a BCRP inhibitor. OJJAARA may increase exposure of BCRP substrates, which may increase the risk of BCRP substrate adverse reactions. When administered concomitantly with OJJAARA, initiate rosuvastatin (BCRP substrate) at 5 mg and do not increase to more than 10 mg once daily. Dose adjustment of other BCRP substrates may also be needed. Follow approved product information recommendations for other BCRP substrates.

Pregnancy

- Available data in pregnant women are insufficient. OJJAARA should only be used during pregnancy if the expected benefits to the mother outweigh the potential risks to the fetus.

Lactation

- It is not known whether OJJAARA is excreted in human milk. Because of the potential for serious adverse reactions in a breastfed child, patients should not breastfeed during treatment with OJJAARA, and for at least 1 week after the last dose of OJJAARA.

Females and Males of Reproductive Potential

- Advise females of reproductive potential who are not pregnant to use highly effective contraception during therapy and for at least 1 week after the last dose of OJJAARA.

Hepatic Impairment

- Momelotinib exposure increased with severe hepatic impairment (Child-Pugh C). The recommended starting dose of OJJAARA in patients with severe hepatic impairment (Child-Pugh C) is 150 mg orally once daily. No dose modification is recommended for patients with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B).

Please see Brief Summary of the full Prescribing Information for OJJAARA on the following pages.

References: 1. OJJAARA (momelotinib). Prescribing Information. GSK; 2025.
2. Chifotides HT, Bose P, Verstovsek S. Momelotinib: an emerging treatment for myelofibrosis patients with anemia. *J Hematol Oncol.* 2021;15(1):7. doi:10.1186/s13045-021-01157-4

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

OJJAARA (momelotinib) tablets, for oral use

The following is a brief summary only; see full prescribing information for complete product information available at www.OJJAARAhcp.com

1 INDICATIONS AND USAGE

OJJAARA is indicated for the treatment of intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF [post-polycythemia vera (PV) and post-essential thrombocythemia (ET)], in adults with anemia.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Infections

Serious (including fatal) infections (e.g., bacterial and viral, including COVID-19) occurred in 13% of patients treated with OJJAARA. Infections regardless of grade occurred in 38% of patients treated with OJJAARA [see *Adverse Reactions (6.1)*]. Delay starting therapy with OJJAARA until active infections have resolved. Monitor patients receiving OJJAARA for signs and symptoms of infection and initiate appropriate treatment promptly.

Hepatitis B Reactivation

Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine transaminase (ALT) or aspartate transaminase (AST), have been reported in patients with chronic hepatitis B virus (HBV) infection taking Janus Kinase (JAK) inhibitors, including OJJAARA. The effect of OJJAARA on viral replication in patients with chronic HBV infection is unknown. In patients with HBV infections, check hepatitis B serologies prior to starting OJJAARA. If HBsAg and/or anti-HBc antibody is positive, consider consultation with a hepatologist regarding monitoring for reactivation versus prophylactic hepatitis B therapy. Patients with chronic HBV infection who receive OJJAARA should have their chronic HBV infection treated and monitored according to clinical HBV guidelines.

5.2 Thrombocytopenia and Neutropenia

OJJAARA can cause thrombocytopenia and neutropenia [see *Adverse Reactions (6.1)*].

New or worsening thrombocytopenia, with platelet count less than $50 \times 10^9/L$, was observed in 20% of patients treated with OJJAARA. Eight percent of patients treated with OJJAARA had baseline platelet counts less than $50 \times 10^9/L$. Severe neutropenia, absolute neutrophil count (ANC) less than $0.5 \times 10^9/L$, was observed in 2% of patients treated with OJJAARA.

Assess complete blood counts (CBC), including platelet and neutrophil counts, before initiating treatment and periodically during treatment as clinically indicated. Interrupt dosing or reduce the dose for thrombocytopenia or neutropenia [see *Dosage and Administration (2.4)* of full prescribing information].

5.3 Hepatotoxicity

Two of the 993 patients with MF who received at least one dose of OJJAARA in clinical trials experienced reversible drug-induced liver injury. Overall, new or worsening elevations of ALT and AST (all grades) occurred in 23% and 24%, respectively, of patients treated with OJJAARA; Grade 3 and 4 transaminase elevations occurred in 1% and 0.5% of patients, respectively. New or worsening elevations of total bilirubin occurred in 16% of patients treated with OJJAARA. All total bilirubin elevations were Grades 1-2. The median time to onset of any grade transaminase elevation was 2 months, with 75% of cases occurring within 4 months.

Delay starting therapy in patients presenting with uncontrolled acute and chronic liver disease until apparent causes have been investigated and treated as clinically indicated. When initiating OJJAARA, refer to dosing in patients with hepatic impairment [see *Dosage and Administration (2.3)* of full prescribing information].

Monitor liver tests at baseline, every month for 6 months during treatment, then periodically as clinically indicated. If increases in ALT, AST or bilirubin related to treatment are suspected, modify OJJAARA dosage based upon Table 1 [see *Dosage and Administration (2.4)* of full prescribing information].

5.4 Severe Cutaneous Adverse Reactions (SCARs)

Severe cutaneous adverse reactions, including toxic epidermal necrolysis (TEN), have been observed in some patients treated with OJJAARA. If signs or symptoms of severe cutaneous reactions occur, interrupt OJJAARA until the etiology of the reaction has been determined. Consider early consultation with a dermatologist for evaluation and management. If etiology is considered to be associated with OJJAARA, permanently discontinue and do not reintroduce OJJAARA in patients who have experienced SCARs or other life-threatening cutaneous reactions during OJJAARA treatment.

5.5 Major Adverse Cardiovascular Events (MACE)

Another JAK inhibitor increased the risk of MACE, including cardiovascular death, myocardial infarction, and stroke [compared with those treated with tumor necrosis factor (TNF) blockers] in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OJJAARA, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Inform patients receiving OJJAARA of the symptoms of serious cardiovascular events and the steps to take if they occur.

5.6 Thrombosis

Another JAK inhibitor increased the risk of thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis (compared with those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated.

Evaluate patients with symptoms of thrombosis and treat appropriately.

5.7 Malignancies

Another JAK inhibitor increased the risk of lymphoma and other malignancies excluding nonmelanoma skin cancer (NMSC) (compared with those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which OJJAARA is not indicated. Current or past smokers were at increased risk.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with OJJAARA, particularly in patients with a known malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Risk of Infections and Hepatitis B Reactivation [see *Warnings and Precautions (5.1)*]
- Thrombocytopenia and Neutropenia [see *Warnings and Precautions (5.2)*]
- Hepatotoxicity [see *Warnings and Precautions (5.3)*]
- Severe Cutaneous Adverse Reactions [see *Warnings and Precautions (5.4)*]
- Major Adverse Cardiovascular Events [see *Warnings and Precautions (5.5)*]
- Thrombosis [see *Warnings and Precautions (5.6)*]
- Malignancies [see *Warnings and Precautions (5.7)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of OJJAARA was evaluated in 215 patients in 2 clinical trials (MOMENTUM and SIMPLIFY-1 anemic subgroup [hemoglobin (Hb) <10 g/dL]) [see *Clinical Studies (14)* of full prescribing information].

MOMENTUM

Patients in the MOMENTUM trial had been previously treated with a JAK inhibitor and were randomly assigned 2:1 to receive double-blind OJJAARA 200 mg orally once daily (n = 130) or danazol 300 mg orally twice daily (n = 65) for 24 weeks, after which they were eligible to receive open-label OJJAARA in an extended treatment phase. Among patients who received OJJAARA, 72% were exposed for 24 weeks or longer and 52% were exposed for 48 weeks or longer [see *Clinical Studies (14)* of full prescribing information].

Serious adverse reactions occurred in 35% of patients who received OJJAARA during the randomized treatment period of the MOMENTUM trial; the most common serious adverse reactions ($\geq 2\%$) included bacterial infection (8%), viral infection (5%), hemorrhage (4%), acute kidney injury (3%), pneumonia (3%), pyrexia (3%), thrombosis (3%), syncope (2%), thrombocytopenia (2%), and renal and urinary tract infection (2%). Fatal adverse reactions occurred in 12% of patients who received OJJAARA; the most common ($\geq 2\%$) fatal adverse reaction was viral infection (5%).

Permanent discontinuation of OJJAARA due to an adverse reaction occurred in 18% of patients during the randomized treatment period of the MOMENTUM trial. Adverse reactions that resulted in permanent discontinuation ($\geq 2\%$) included viral infection (2%) and thrombocytopenia (2%). Dosage reduction or treatment interruption due to an adverse reaction occurred in 34% of patients. Adverse reactions requiring dosage reduction and/or treatment interruption ($\geq 2\%$) included thrombocytopenia (13%), bacterial infection (2%), diarrhea (2%), and neutropenia (2%).

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6 ADVERSE REACTIONS (cont'd)

6.1 Clinical Trials Experience (cont'd)

Among the 130 patients treated with OJJAARA during the randomized treatment period of MOMENTUM, the most common adverse reactions ($\geq 20\%$) were thrombocytopenia, diarrhea, hemorrhage, and fatigue (Table 1).

Table 1: Adverse Reactions Occurring in $\geq 5\%$ of Patients Receiving OJJAARA during Randomized Treatment in MOMENTUM

Adverse Reaction	OJJAARA n = 130		Danazol ^a n = 65	
	All Grades ^b %	Grade ≥ 3 %	All Grades %	Grade ≥ 3 %
Thrombocytopenia ^c	28	22	17	12
Diarrhea ^c	22	0	9	2
Hemorrhage ^c	22	2	18	8
Fatigue ^c	21	2	20	5
Nausea ^c	16	2	9	3
Bacterial infection ^{c,d}	15	8	18	8
Abdominal pain ^c	13	1	18	3
Viral infection ^{c,d}	12	5	3	0
Pruritus ^c	11	2	11	0
Elevated liver enzymes ^c	10	2	9	3
Pyrexia ^c	10	2	8	0
Cough ^c	8	0	5	0
Paresthesia ^c	8	1	2	0
Dizziness ^c	8	2	2	0
Vomiting ^c	8	1	0	0
Rash ^c	6	0	11	0
Renal and urinary tract infection ^{c,d}	6	2	11	5
Arrhythmia ^c	5	1	6	2
Neutropenia	5	5	3	3

^aStudy was not designed to evaluate meaningful comparisons of the incidence of adverse reactions across treatment groups.

^bAdverse reactions graded using CTCAE v.5.

^cGrouped term includes other related terms.

^dExcludes opportunistic infections.

SIMPLIFY-1

Patients in the SIMPLIFY-1 trial were JAK inhibitor naïve and randomly assigned 1:1 to receive double-blind OJJAARA 200 mg orally once daily (n = 215) or ruxolitinib 5 to 20 mg orally twice daily (n = 217). Upon completion of the double-blind treatment phase, all patients were eligible to receive OJJAARA during the open-label phase. The safety of OJJAARA was evaluated in the population of patients with MF who were anemic at study entry. SIMPLIFY-1 enrolled 180 anemic patients who received OJJAARA (n = 85) or ruxolitinib (n = 95). Among these anemic patients who received OJJAARA, 78% were exposed for 24 weeks or longer and 61% were exposed for 48 weeks or longer [see *Clinical Studies (14) of full prescribing information*].

Serious adverse reactions occurred in 28% of the anemic patients who received OJJAARA during the randomized treatment period of the SIMPLIFY-1 trial; the most common serious adverse reactions ($\geq 2\%$) included bacterial infection (7%), pneumonia (6%), heart failure (4%), arrhythmia (2%), and respiratory failure (2%). A fatal adverse reaction (bacterial infection) occurred in 1 patient who received OJJAARA.

Permanent discontinuation of OJJAARA due to an adverse reaction occurred in 19% of the anemic patients during the randomized treatment period of the SIMPLIFY-1 trial. Adverse reactions that resulted in permanent discontinuation of OJJAARA ($\geq 2\%$) included bacterial infection (2%), dizziness (2%), fatigue (2%), hypotension (2%), and thrombocytopenia (2%). Dosage reductions or treatment interruptions of OJJAARA due to an adverse reaction occurred in 21% of patients. Adverse reactions requiring dosage reduction and/or treatment interruption ($\geq 2\%$) were thrombocytopenia (8%), pneumonia (4%), bacterial infection (2%), abdominal pain (2%), elevated liver enzymes (2%), and hypotension (2%).

Among the 85 anemic patients treated with OJJAARA during the randomized treatment period of SIMPLIFY-1, the most common adverse reactions ($\geq 20\%$) were dizziness, fatigue, bacterial infection, hemorrhage, thrombocytopenia, diarrhea, and nausea (Table 2).

Table 2: Adverse Reactions Occurring in $\geq 5\%$ of Anemic Patients Receiving OJJAARA during Randomized Treatment in SIMPLIFY-1

Adverse Reactions	OJJAARA n = 85 Baseline Hb <10 g/dL		Ruxolitinib ^a n = 95 Baseline Hb <10 g/dL	
	All Grades ^b %	Grade ≥ 3 %	All Grades %	Grade ≥ 3 %
Dizziness ^c	24	1	15	2
Fatigue ^c	22	0	25	1
Bacterial infection ^{c,d}	21	8	12	2
Hemorrhage ^c	21	1	18	2
Thrombocytopenia ^c	21	11	34	6
Diarrhea ^c	20	1	20	1
Nausea ^c	20	0	3	1
Abdominal pain ^c	18	1	14	1
Cough ^c	14	0	11	0
Hypotension ^c	14	2	0	0
Pain in extremity	12	0	5	0
Pyrexia ^c	12	1	11	0
Rash ^c	12	0	3	0
Renal and urinary tract infection ^{c,d}	12	1	4	0
Elevated liver enzymes ^c	11	4	9	0
Headache ^c	11	0	16	0
Peripheral edema	11	0	8	0
Arrhythmia ^c	8	2	2	1
Paresthesia ^c	8	0	3	0
Pneumonia ^c	8	8	5	3
Vomiting ^c	8	0	5	0
Back pain	7	1	2	0
Viral infection ^{c,d}	6	0	13	2
Vitamin B1 deficiency	6	0	7	0

^aStudy was not designed to evaluate meaningful comparisons of the incidence of adverse reactions across treatment groups.

^bAdverse reactions graded using CTCAE v.4.03.

^cGrouped term includes other related terms.

^dExcludes opportunistic infections.

Other Adverse Reactions

Clinically relevant adverse reactions occurring in $<5\%$ of anemic patients in the MOMENTUM and SIMPLIFY-1 studies include:

Eye Disorders: Blurred vision.

Infections and Infestations: Fungal infection (excludes opportunistic infections).

Nervous System Disorders: Neuralgia, peripheral neuropathy, peripheral motor neuropathy, polyneuropathy.

Vascular Disorders: Flushing.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of OJJAARA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Skin and Subcutaneous Tissue Disorders: Toxic epidermal necrolysis (TEN).

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on OJJAARA

Organic Anion Transporting Polypeptide (OATP)1B1/B3 Inhibitors

Momelotinib is an OATP1B1/B3 substrate. Concomitant use with an OATP1B1/B3 inhibitor increases momelotinib maximal concentrations (C_{max}) and area under the concentration-time curve (AUC) [see *Clinical Pharmacology (12.3) of full prescribing information*], which may increase the risk of adverse reactions with OJJAARA. Monitor patients concomitantly receiving an OATP1B1/B3 inhibitor for adverse reactions and consider OJJAARA dose modifications [see *Dosage and Administration (2.4) of full prescribing information*].

7.2 Effect of OJJAARA on Other Drugs

Breast Cancer Resistance Protein (BCRP) Substrates

Momelotinib is a BCRP inhibitor. OJJAARA may increase exposure of BCRP substrates, which may increase the risk of BCRP substrate adverse reactions [see *Clinical Pharmacology (12.3) of full prescribing information*]. When administered concomitantly with OJJAARA, initiate rosuvastatin (BCRP substrate) at 5 mg and do not increase to more than 10 mg once daily. Dose

(continued on next page)

7 DRUG INTERACTIONS (cont'd)

7.2 Effect of OJJAARA on Other Drugs (cont'd)

adjustment of other BCRP substrates may also be needed. Follow approved product information recommendations for other BCRP substrates.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data on the use of OJJAARA in pregnant women are insufficient to determine whether there is a drug-associated risk for major birth defects or miscarriage. Based on animal reproduction studies conducted in rats and rabbits, momelotinib may cause embryo-fetal toxicity at exposures lower than the expected exposure in patients receiving 200 mg once daily (see Data). OJJAARA should only be used during pregnancy if the expected benefits to the mother outweigh the potential risks to the fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data: In an embryofetal development study, pregnant rats received momelotinib 2, 6 or 12 mg/kg/day orally, during the period of organogenesis (Gestation Day 6 to 17). Embryo-fetal toxicity (embryonic death, soft tissue anomalies, skeletal variations, and lower mean fetal body weights) was observed at 12 mg/kg (in the presence of maternal toxicity). Skeletal variations were observed (in the absence of maternal toxicity) at 6 mg/kg/day at exposures 3.5 times the exposure at the recommended human dose of 200 mg daily based on combined momelotinib and M21 (a major human metabolite) AUC. No developmental toxicity was observed at 2 mg/kg/day at exposures equivalent to the recommended dose (based on combined momelotinib and M21 AUC).

In an embryofetal developmental study, pregnant rabbits received momelotinib at 7.5, 30 or 60 mg/kg/day orally during the period of organogenesis (Gestation Day 7 to 20). Momelotinib was associated with maternal toxicity at 60 mg/kg/day, which resulted in reduced mean fetal weight, delayed bone ossification, and an abortion at less than the exposure at the recommended dose (based on combined momelotinib and M21 AUC). No developmental toxicity was observed at lower doses tested in rabbits.

In a pre- and post-natal development study, pregnant rats received momelotinib 2, 6 or 12 mg/kg/day orally from organogenesis through lactation (Gestation Day 6 to lactation Day 20). Decreased pup body weights and embryo-lethality were observed in the dams administered 6 and 12 mg/kg/day. Pup survival was significantly reduced in the 12 mg/kg/day group from birth to Day 4 of lactation. Momelotinib exposure in dams at 12 mg/kg and 6 mg/kg were approximately 2 times the exposure at the recommended dose (based on combined momelotinib and M21 AUC). The exposure in dams at the No Observed Adverse Effect Level (NOAEL) dose of 2 mg/kg was less than the exposure at the recommended dose (based on combined momelotinib and M21 AUC).

8.2 Lactation

Risk Summary

There are no data on the presence of momelotinib or its metabolites in human milk, the effects on the breastfed child, or the effects on milk production. It is not known whether OJJAARA is excreted in human milk. Momelotinib was present in rat pups following nursing from treated dams with adverse effects observed in the offspring. When a drug is present in animal milk, it is likely that the drug will be present in human milk. Because of the potential for serious adverse reactions in a breastfed child, patients should not breastfeed during treatment with OJJAARA, and for at least 1 week after the last dose of OJJAARA.

Data

Animal Data: In a pre- and postnatal development study, momelotinib was administered orally to rats during the lactation period; the drug was detected in plasma of nursing pups, which adversely affected pup survival.

8.3 Females and Males of Reproductive Potential

Contraception

Advise females of reproductive potential who are not pregnant to use highly effective contraception during therapy and for at least 1 week after the last dose of OJJAARA.

8.5 Geriatric Use

There were 275 patients aged 65 years and older in the clinical studies for MF [see Clinical Studies (14) of full prescribing information]. Of the total number of OJJAARA-treated patients in these studies, 163/216 (75%) were aged 65 years and older, and 63/216 (29%) were aged 75 years and older. No overall differences in safety or effectiveness of OJJAARA have been observed between patients aged 65 years and older and younger adult patients.

8.6 Hepatic Impairment

The recommended starting dose of OJJAARA in patients with severe hepatic impairment (Child-Pugh C) is 150 mg orally once daily [see Dosage and Administration (2.3) of full prescribing information]. No dose modification is

recommended for patients with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B).

Momelotinib is extensively metabolized [see Clinical Pharmacology (12.3) of full prescribing information]. Momelotinib exposure increased with severe hepatic impairment (Child-Pugh C). No clinically significant changes in momelotinib exposure were observed in subjects with mild hepatic impairment (Child-Pugh A) or moderate hepatic impairment (Child-Pugh B) [see Clinical Pharmacology (12.3) of full prescribing information].

10 OVERDOSAGE

There is no known antidote for overdose with OJJAARA. If overdose is suspected, the patient should be monitored for signs or symptoms of adverse reactions or effects, and appropriate supportive treatment should be instituted immediately. Further management should be as clinically indicated. Hemodialysis is not expected to enhance the elimination of momelotinib.

Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA approved patient labeling (Patient Information).

Infections

Inform patients that OJJAARA can increase the risk of infections (including COVID-19) and instruct them to promptly report to their healthcare provider any signs and symptoms of infection [see Warnings and Precautions (5.1)].

Thrombocytopenia and Neutropenia

Inform patients that OJJAARA can cause thrombocytopenia and neutropenia, and of the need to monitor complete blood count, including platelet and neutrophil counts, before and during treatment. Advise patients to observe for and report any bleeding to their healthcare provider [see Warnings and Precautions (5.2)].

Hepatotoxicity

Inform patients that OJJAARA can cause hepatotoxicity, and of the need to monitor liver blood tests before and during treatment [see Warnings and Precautions (5.3)].

Severe Cutaneous Adverse Reactions (SCARs)

Inform patients that SCARs have been reported in some patients treated with OJJAARA and instruct them to promptly report any signs and symptoms of SCARs to their healthcare provider [see Warnings and Precautions (5.4)].

Major Adverse Cardiovascular Events (MACE)

Advise patients that events of MACE including myocardial infarction, stroke, and cardiovascular death have been reported in clinical studies with another JAK inhibitor used to treat rheumatoid arthritis, a condition for which OJJAARA is not indicated. Advise patients, especially current or past smokers and patients with other cardiovascular risk factors, to be alert for the development of signs and symptoms of cardiovascular events and to report them to their healthcare provider [see Warnings and Precautions (5.5)].

Thrombosis

Advise patients that events of deep vein thrombosis (DVT) and pulmonary embolism (PE) have been reported in clinical studies with another JAK-inhibitor used to treat rheumatoid arthritis, a condition for which OJJAARA is not indicated. Advise patients to tell their healthcare provider if they develop any signs or symptoms of a DVT or PE [see Warnings and Precautions (5.6)].

Malignancies

Advise patients, especially current or past smokers, that lymphoma and other malignancies (excluding non-melanoma skin cancers (NMSC)) have been reported in clinical studies with another JAK inhibitor used to treat rheumatoid arthritis, a condition for which OJJAARA is not indicated [see Warnings and Precautions (5.7)].

Pregnancy

- Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their prescriber of a known or suspected pregnancy [see Use in Specific Populations (8.1)].
- Advise females of reproductive potential who are not pregnant to use highly effective contraception during therapy and for 1 week after the last dose of OJJAARA [see Use in Specific Populations (8.3)].

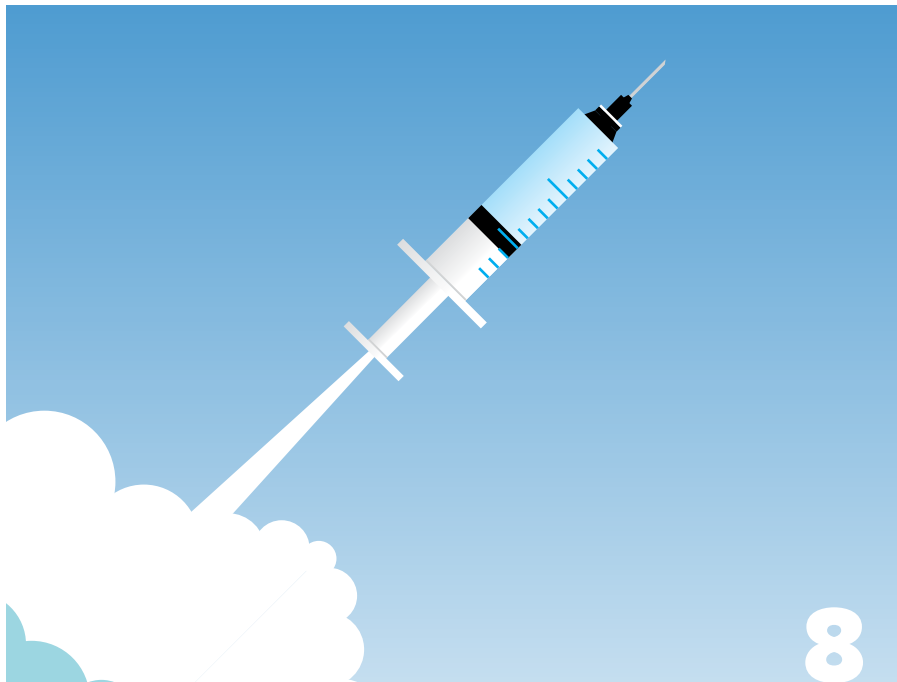
Lactation

Advise patients not to breastfeed during treatment with OJJAARA and for at least 1 week after the last dose of OJJAARA [see Use in Specific Populations (8.2)].

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Signaling Immunity: The Rise of Cancer Vaccines in Hematologic Malignancies

Personalized cancer vaccines use dendritic cells or neoantigens to stimulate the immune system to recognize and attack cancer cells.

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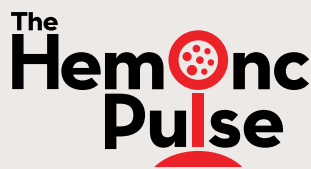
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GET TO KNOW

Alan Skarbnik, MD

Dr. Skarbnik wears many titles: hematologist oncologist, rock musician, and father of three.

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Get to Know

Learn more about the leaders, innovators, and educators in hematologic oncology



Alan Skarbnik, MD

Alan Skarbnik, MD, wears many titles: hematologist oncologist, rock musician, and father of three.

By Melissa Badamo



Photo Courtesy of Alan Skarbnik, MD

A jack of all trades, Dr. Skarbnik's day-to-day life consists of playing three instruments in a rock band, treating patients with chronic lymphocytic leukemia (CLL) and lymphoma, and researching curative immunotherapies. But before leading clinical trials and building Novant Health's CAR-T program, the clinician-researcher first developed an interest in hematology oncology after a close friend's father died of lymphoma.

"The clinical and humanistic aspects of hematologic malignancies sparked my interest at first, then I started looking into the scientific aspect," he said.

Hailing from São Paulo, Brazil, Dr. Skarbnik attended medical school at the Universidade de São Paulo Faculdade de Medicina before moving to the United States to continue his education. After completing an internal medicine residency at St. Luke's-Roosevelt Hospital Center, he landed a hematology-oncology fellowship at the Fox Chase Cancer Center from 2010-2013 and then a hematopoietic stem cell transplantation fellowship at the City of Hope National Medical Center from 2013-2014.

At the time, new developments were gaining momentum in hematologic malignancies with

the study of targeted agents such as ibrutinib, he recalled. Now, the field has witnessed a surge of cellular therapies and bispecific antibodies and a shift from hematopoietic stem cell transplant to chimeric antigen receptor (CAR) T-cell therapy in lymphomas.

"It was very interesting to see a shift from traditional, broader, and more aggressive chemotherapy and radiation therapy approaches to more nuanced and targeted therapies," he said. "It was a completely new field."

New Beginnings: A Research Career in CLL

Now, Dr. Skarbnik serves as director of the Lymphoma and CLL Program and director of the Immune-Effector Cell Therapeutics program at Novant Health Cancer Institute in Charlotte, North Carolina. He also served as a clinical investigator on many trials, including the ELEVATE-TN and TRANSCEND FL trials.

The ELEVATE-TN trial showed that acalabrutinib plus obinutuzumab improves survival compared with chemoimmunotherapy for patients with treatment-naïve CLL, and TRANSCEND-FL showed that

lisocabtagene maraleucel CAR T-cell therapy is safe and effective in follicular lymphoma.

"The ELEVATE-TN trial started around the time ibrutinib was approved for relapsed disease, but not yet approved for frontline therapy," Dr. Skarbnik said. "We were already starting to understand that ibrutinib, which is a great drug and completely changed how we treat CLL, was not necessarily well-tolerated by everyone. This was a large phase 3 trial establishing acalabrutinib as one of the options of standard of care for treating CLL in the frontline setting."

Participating in the ELEVATE-TN trial as an investigator opened doors for exciting opportunities in his research career. "It was a great experience," he said. "I started as a site PI [principal investigator] for this study during my first job shortly after I completed fellowship. It was the first large trial I had the opportunity to participate in as an investigator."

Rather than being at a traditional academic setting, Dr. Skarbnik describes Novant Health as a nonacademic, hospital system-based practice. "Sometimes, being outside of a university is more difficult in terms of producing clinical research," he

said. “Now, we changed a lot, where patients want to be close to where they live without traveling much. A lot of larger practices that have a clinical research program are thriving, because we have local patients and can improve access to clinical trials for them. This particular study showed me that this was possible and opened a lot of doors for me to be an investigator in other trials outside of a traditional academic model, and that is how I practice today in my current job as well.”

From Bench to Bedside: Building the CAR-T Program at Novant Health

With a large team of collaborators, Dr. Skarbnik and

Forming Patient Connections: From Patient to Bandmate

For any oncologist, patients are a large part of their life and career. For Dr. Skarbnik, a former patient is also the lead singer of his rock band, “Midlife Crisis.”

“We were looking for a singer, and she knew I was putting a new band together on her last visit,” he recalled. “After 5 years of treatment, I told her, ‘You’re cured, you can go live your life.’ She asked me about my band and auditioned in the office on her last visit, and now we’re in a band together. It’s very fun.”

A multi-instrumentalist, Dr. Skarbnik plays keyboards, saxophone, and guitar in the band.

“Even if we cannot eliminate the disease molecularly in patients forever, they may never need treatment again in their lifetime.”



his team at Novant Health successfully built a CAR T-cell program from scratch during the height of the COVID-19 pandemic in 2020, a feat he considers the proudest moment of his career.

“I was recruited to North Carolina to work in a nonacademic environment that did not have a cancer institute established yet,” he said. “There were two primary goals: (1) to develop a lymphoma and CLL research program; and (2) to develop a CAR T-cell program in a place that wasn’t yet set up for that at all. We were able to perform our first CAR-T infusion in September 2020, right in the middle of the pandemic, and open a program when the world was falling apart.”

Five years later, the first patient treated with CAR T-cell therapy at Novant Health continues to do well and is still in remission.

“The moment we gave the patient our first CAR-T cells in this program was the proudest moment of my career,” he reflected. “That was the apex of several years of training of working in other places, learning, understanding, building something from the ground up in a place that was unexpected to be able to do so. And, we were able to do that very successfully.”

“Music is a passion and a good outlet from our day-to-day work,” he said, a Rolling Stones poster displayed on the blue wall behind him. “It’s good to have a moment reserved every week to spend time with friends and do something together outside the stresses of work.”

Dr. Skarbnik previously co-owned an 1980s nightclub in Brazil, and his former band even recorded and played on the radio in Brazil.

Dr. Skarbnik’s other hobbies include grilling, baking, pizza-making, and traveling with his family. His three children—aged 13, 10, and 8 years—hope to follow in his footsteps and join the medical field one day.

Less Chemotherapy, More Immunotherapy

Throughout his career, Dr. Skarbnik has witnessed the approval of ibrutinib, the introduction of CAR-T and bispecific antibodies, and other major developments. Looking into the future, he hopes the field transitions away from chemotherapy and towards immunotherapy.

“I expect to see us continue to transition away from traditional cytotoxic chemotherapy for lymphomas and CLL, which is harder to tolerate. A number of patients

may not necessarily be eligible for chemotherapy and I’d like to see the field transition more into immunotherapy, immune effector cell therapy, and targeted therapy approaches in earlier lines of treatment” he said. “The second thing we’re going to start seeing is better, less toxic immune effector cell therapies and newer, more streamlined CAR-Ts that will decrease the length of time between a patient needing a treatment and being able to receive it.”

Lastly, Dr. Skarbnik hopes to see one major feat in his lifetime: a cure for all lymphomas.

“I do believe we’re already curing some patients with diseases that were previously thought to be incurable, particularly with CAR T-cell therapy for follicular lymphoma and marginal zone lymphoma,” he said. “There are clinical trials looking at using bispecifics very early on in the treatment of follicular lymphoma when patients have a low burden of disease. I think we’re going to change the landscape of ‘incurable’ diseases to becoming curable diseases. Even if we cannot eliminate the disease molecularly in patients forever, they may never need treatment again in their lifetime. That, functionally, is equivalent to a cure.”



SIGNALING IMMUNITY:

The Rise of Cancer Vaccines in Hematologic Malignancies

By Melissa Badamo

Once upon a time, a vaccine for cancer may have sounded like an invention straight from a science fiction novel. Now, cancer vaccines that stimulate the immune system to attack cancer cells and prevent disease recurrence are a welcoming reality for some patients with hematologic malignancies.

Over the past 2 decades, immunotherapies like chimeric antigen receptor (CAR) T-cell therapy, monoclonal and bispecific antibodies, antibody-drug conjugates, and immune checkpoint inhibitors have emerged as treatment pathways for patients with hematologic malignancies and have dramatically improved outcomes for some patients. However, these immunotherapies come with limitations as many patients develop resistance or do not respond to treatment, highlighting the ongoing need for new therapies and combinational strategies.¹ Personalized cancer vaccines aim to overcome these challenges by “training” the immune system to target low volume disease and induce a stronger immune response.¹

Dendritic Cell-Based Cancer Vaccines

A research team led by **David Avigan, MD**, director of the Cancer Center at Beth Israel Deaconess Medical Center (BIDMC) and professor of medicine at Harvard Medical School (HMS); and **Jacalyn M. Rosenblatt, MD**, associate chief of the Division of Hematological Malignancies at BIDMC and associate professor of medicine at HMS, studied a personalized dendritic cell-based cancer vaccine in multiple myeloma and translated their laboratory findings into a series of

clinical trials. Developed by fusing patient-derived myeloma cells with autologous dendritic cells using polyethylene glycol, dendritic cell-based vaccines work by stimulating immune responses that identify and selectively eliminate cancer cells.²

“We have a vaccine model where we generate vaccines for each person from their own cells,” Dr. Rosenblatt told *Blood Cancers Today*. “Cancer cells don’t do a good job at stimulating the immune system to recognize them. In contrast, dendritic cells are very good at stimulating the immune system and can be used as a backbone for generating cancer vaccines.”

By taking tumor cells from a patient, Dr. Rosenblatt and her team can generate dendritic cells from a patient’s blood, then fuse the tumor cells to the dendritic cells to create a fusion cell. The fusion cell contains aspects of the patient’s tumor that can then be presented by the dendritic cell, she explained.

“The notion of a vaccine has to do with reeducating the immune system to see a particular target, in this case a cancer cell, as foreign,” added Dr. Avigan. “There are a variety of antigens that have been discovered over time, either on tumor cells or normal cells. Some antigens, known as neoantigens, come from mutations in the tumor cell. These have the advantage of being more foreign and may induce a more productive immune response, because our immune system is tailored not to target our own body. The less ‘self’ it is, the more targetable.”

However, one challenge is that tumors are heterogeneous and don’t uniformly express targets, Dr. Avigan noted.

“Therefore, cancer can escape any kind of therapy because you might hit one population that’s vulnerable, but then there’s another population that isn’t,” he explained. “Dendritic cell-tumor fusion-based vaccines attempt to overcome these challenges by taking whole cells from the patient and using that as antigens. We’re essentially letting the body make a diverse, polyclonal response. It hits multiple targets, and we’re letting the body tell us which targets are most recognizable to us.”

Preclinical models, which showed that dendritic cell-based vaccines can induce strong immune responses and eradicate disease in mice, paved the way for phase 1 and 2 clinical trials. In the phase 1 trial, vaccination with up to 4×10^6 fusion cells was feasible and well tolerated following autologous hematopoietic cell transplant (HSCT) in patients with myeloma who received at least one prior treatment. Common toxicities, like a rash or reaction at the injection site, were modest.²

“The main category of toxicities we worry about are ones where the immune system is overheated and you get side effects that cause problems for the patient themselves against normal tissues,” Dr. Avigan said. “That, historically with our vaccine and many others, has not been a huge issue. We don’t see an uproar of the immune system like with other immunotherapies, such as CAR T-cells or bispecific T cell engagers.”

In the phase 2 trial, the vaccine, when combined with lenalidomide after HSCT, was associated with a significant increase in circulating multiple myeloma-reactive lymphocytes, suggesting tumor-specific immunity.³

“We saw a clear expansion of T-cells, and they persist,” Dr. Avigan said. “We were trying to stimulate tumor-specific effector cells, or T cells, to go after the tumor, then circulate as a form of immune surveillance. We were able to generate those cells, and they’re durable.”

A third factor besides safety and immune response is clinical response, Dr. Avigan noted. In the phase 2 study, the dendritic cell fusion vaccine with lenalidomide maintenance did not lead to a statistically significant increase in complete response (CR) rates at 1 year after autologous HSCT compared with control arms.³ A total of 85% of patients in the vaccine arm achieved a CR or very good partial response, compared with 77% in the nonvaccine arm.³

“Vaccines will not be able to take a large amount of disease and shrink it down to nothing,” he continued. “Vaccines are most effective for patients who have already achieved a good degree of response as they try to keep the disease from returning. We think of vaccines as providing memory as a barrier for a disease growing rather than shrinking it from a very large state.”

The 2-year progression-free survival rates also did not demonstrate a statistically significant difference between the vaccine and nonvaccine arms at 79% and 88%, respectively. Larger studies are needed to fully assess the vaccine’s clinical impact.³

“We’re waiting to understand this clear immune effect and what it means clinically,” Dr. Avigan added. “We have some hints that maybe we can prevent relapse in high-risk settings, but we still need to learn more about that.”

Personalized Neoantigen Vaccines

NeoVax in Chronic Lymphocytic Leukemia (CLL)

In addition to dendritic cells, neoantigens provide another way to stimulate the immune system to target cancer cells.

Researchers at the Dana-Farber Cancer Institute are developing a personalized neoantigen vaccine called “NeoVax” for patients with treatment-naïve, asymptomatic CLL without *IGHV* mutations. NeoVax works by scanning the genetic information inside cancer cells to identify epitopes within neoantigens, proteins on cancer cells caused by genetic mutations.⁴ By mixing copies of these neoantigens with Poly ICLC, an experimental immunomodulator, the vaccine tells the immune system to attack CLL cells containing the mutations.^{4,5}

A phase 1 study is evaluating the feasibility and safety of NeoVax alone and in combination with two other immunotherapies: cyclophosphamide or pembrolizumab.⁵ Based on initial results presented at the Intercepting Blood Cancers meeting in early 2025, NeoVax successfully triggered an immune response by activating CD4+ and CD8+ T-cells to target CLL.⁶ Although NeoVax monotherapy effectively reduced CLL cells, patients still progressed 10 months after NeoVax monotherapy, therefore requiring additional venetoclax and obinutuzumab treatment. Adding cyclophosphamide boosted the vaccine’s efficacy by sustaining CLL cell reduction.⁶

PGV001 in Multiple Myeloma

PGV001, a personalized genome vaccine (PGV) targeting each patient’s unique disease, induced strong

immune responses across multiple malignancies, including multiple myeloma.¹ Like NeoVax, this approach utilizes multiple peptides to signal the immune system to recognize and attack neoantigens while preventing the cancer from returning.¹

A study published in *Cancer Discovery* tested this strategy in 13 patients with five different cancers, including three patients with myeloma. Patients had a high risk of disease recurrence despite receiving prior standard treatments. The vaccine was administered over 27 weeks, and all vaccinated patients developed targeted T-cell and B-cell responses.⁷ Of the six patients who survived at a 5-year follow-up, three remain tumor-free.¹

Although PGV001 is safe and feasible with no serious side effects, future studies are planned to confirm these findings in a larger population.¹

NeoAg Peptide Vaccine in Smoldering Myeloma

Personalized neoantigen vaccines are also being studied to prevent progression from smoldering myeloma to multiple myeloma.

A single center, investigator-initiated study investigated the feasibility, safety, and efficacy of a personalized NeoAg peptide vaccine with or without lenalidomide in 30 patients with high- or intermediate- risk smoldering myeloma. The researchers used tumor sequencing to identify the most highly expressed patient-specific RNA mutations, then successfully immunized all 30 patients for six treatment cycles. Ten patients received the NeoAg peptide vaccine alone (cohort 1), while 20 patients received the vaccine in combination with lenalidomide to enhance immune response (cohort 2). The study team evaluated immune responses using bone marrow and peripheral blood samples.⁸

The vaccine was safe, with no significant dose limiting toxicities observed. All ten patients in cohort 1 achieved stable disease, but two patients progressed to myeloma, and eight patients continue to be observed. In cohort 2, patients either achieved a partial response, minimal response, or achieved stable disease, with five patients progressing to myeloma.⁸

However, immune responses with the NeoAg peptide vaccine waned over time, either due to patient tolerance or decreasing efficacy.⁸

Overcoming Cancer Vaccine Challenges With Combinations

This waning immune response, along with patient relapse, remains a unique challenge in the field of cancer vaccines and immunotherapy. However, Drs. Rosenblatt and Avigan are working to sustain immune responses and prevent relapse by pursuing combination strategies with dendritic cell fusion vaccines.

In preclinical leukemia mouse models, binding stimulated T-cells with a bispecific antibody completely eradicated disease, Dr. Rosenblatt explained, and the combination was more potent than either treatment alone.

An ongoing clinical trial is evaluating elranatamab, a BCMA-directed T-cell engager, in combination with the vaccine in patients with myeloma.⁹ Other clinical trials are looking at the fusion vaccine combined with CAR-T cells.

“CAR T-cells have had a dramatic impact on outcomes for patients with lymphoid malignancies and multiple myeloma,” said Dr. Rosenblatt. “We’ve seen exciting responses in patients with resistant myeloma, which has been incredible. But we know that for most patients, the disease will relapse. A big area of investigation is trying to understand why patients relapse and how combination therapies may help to overcome that risk.”

“The CARs create a very dramatic response, but they disappear within the first month or so. There are very few cells,” added Dr. Avigan. “The immune system has two arms. There’s innate immunity, which is often our first barrier of defense, but it’s usually the memory cells that provide long-term protection.”

According to Dr. Avigan’s research, one notable difference between patients who relapse in the first 6 months versus those who stay in remission is a secondary wave of activation to an adaptive response, which is more T-cell driven around the immune system’s memory response.

Another potential cause of relapse is the emergence of a tumor that no longer expresses the antigen targeted by the CAR-T cell, Dr. Rosenblatt noted. “In combination, the vaccine may stimulate the CAR to be more persistent, it may stimulate the native T-cell response, and it may stimulate a broad T-cell response that can overcome the emergence of clones that no longer express the antigen targeted by the CAR-T cell,” she explained.

Overall, future and ongoing studies will seek to understand how to enhance immune response with novel vaccine combinations while ensuring that the immune system is not overstimulated.

“We may need other agents to work on the tumor microenvironment,” Dr. Avigan concluded. “There are other combinations that involve immune regulatory drugs. Even if we have a good vaccine, we may need to block certain factors that suppress the immune system to make the vaccine more effective.”

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Medicare's Telehealth Policy: A Setback for Cancer Care

By *Rahul Banerjee, MD*, Associate Editor of *Blood Cancers Today* and Host of "The HemOnc Pulse"



Rahul Banerjee, MD
Associate Editor

Over the past year, many patients have asked me whether the seismic shifts in US healthcare policy have affected my day-to-day clinical practice. Up until September 30, the answer had honestly been no—but no longer.

Originally, as of October 1, 2025, Medicare beneficiaries were no longer eligible to receive telehealth services unless they required behavioral health services or live in a rural area.¹ Congress has since extended Medicare telehealth services with the US government reopening after the 43-day shutdown, but only through January 30, 2026.²

As many clinicians are aware, telehealth utilization exploded during the COVID-19 pandemic. In the oncology sphere, these telehealth visits have been rated highly³ by patients living with cancer for many reasons: less "time toxicity" of physically coming to the clinic, lower risk of infection, and the ability to follow up asynchronously to discuss bloodwork and imaging results.

Unfortunately, Medicare coverage for such telehealth visits is provided only through a special Congressional waiver. As a result, older pre-pandemic restrictions around Medicare reimbursement⁴ for telehealth services will return into effect at the end of January.

To say that this lurch has been disheartening for patients would be an understatement. For many of my patients, this change is downright devastating. In general, I can group my patients who prefer telehealth visits with me into three buckets:

1. Telehealth because of a desire for completeness:

Given that I specialize in the treatment of multiple myeloma, many of my patients receive monthly serum protein electrophoresis and serum free light chain bloodwork every 4-8 weeks. These assays can take several days to result. As such, intentionally scheduling a telehealth visit with me 3 to 4 days after their bloodwork can enhance the utility of our discussions.

2. Telehealth because of limited mobility: Many of my patients living with multiple myeloma have quality-of-life impairments related to either their cancer or its treatment: bone pain, peripheral neuropathy, and more. For these patients, an in-person visit is not just an inconvenience; it is a genuine source of physical pain and distress from having to sit in an automobile, navigate city traffic, and walk long distances to arrive within a clinic room.

3. Telehealth out of geographic necessity: About a third of my patients live well beyond driving distance from my clinic, including many who live in other states ranging from Alaska to Montana. These patients have a primary oncologist, of course, but they often look to me to discuss complex questions about how best to manage therapies in the setting of relapsed multiple myeloma. This includes the timing of chimeric antigen receptor T-cell therapy, an advanced but effective treatment modality for blood cancers that is not available at most centers.

Multiple myeloma is primarily a cancer of older adults, and a sizable number of patients living with myeloma thus have Medicare insurance. The sudden removal of these patients' ability to see their oncologists via telehealth has created chaos for clinics across the country as we balance Advance Beneficiary Notices, mainly regarding potential non-reimbursement.

Loss to follow-up is a well-characterized issue⁵ in oncology. Unfortunately, this is generally more common among patients who are more vulnerable due to minority status, low income, long geographic distances, and more—the exact types of patients for whom telehealth visits may be essential to mitigating disparities in cancer care.⁶

As such, my concerns with this shift backward in time with regard to telehealth reimbursement fall on two levels. Firstly, the sudden lack of flexibility regarding telehealth is an immediate problem for patients in my clinic on a day-to-day basis. Secondly, even if the ability to see Medicare recipients by telehealth returns permanently, there is a chance that vulnerable patients living with cancer will not return to my clinic. Loss to follow-up is a pernicious problem for patients with cancer and, in many cases, is a key driver of patient attrition and poor outcomes. I am hopeful that Congressional remediation will prevent any lasting damage from being done for these types of patients, but only time will tell.

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Rethinking Empathy: A Hard Science for Better Communication and Research

By Kimberly Ku, MD

Hematologists understand that patients with and survivors of hematologic malignancies are particularly vulnerable to COVID-19 disease and complications. At the same time, “vaccine hesitancy” can undercut and complicate well-intended hematologic care.¹

A survey conducted by Blood Cancer United reported that even as general distrust in healthcare grew during the COVID-19 pandemic, 89% of patients still trusted their oncologist for information about COVID-19 and vaccines.^{1,2} In addition, social trust in the payer and hospitals may be strongly related to trust in a physician.³ In fact, in a Polish case study of trust restoration in the midst of COVID-19, researchers suggested that mass media information can significantly influence patient trust in some components of healthcare. This influence can occur regardless of whether changes are made to healthcare performance. This implies that an individual hematologist can play a pivotal role as communicator, educator, and engager of their patients and the larger community as well, including members of the media outside the immediate workplace.^{3,4}

Building and maintaining patient trust, therefore, extends beyond delivering accurate information. It requires understanding how patients interpret and emotionally respond to that information. The language used in public health and clinical settings can either strengthen or undermine this trust. Terms that shape discourse, such as vaccine hesitancy, reflect not only scientific perspectives but also social and emotional dynamics that influence patient decision-making.

The first step is to reconsider the phrase *vaccine hesitancy*, a concept explored in depth by medical anthropologists and social scientists.^{5,6} Such a term is laden with assumptions regarding the human complexities of our decision-making process. The person making such a decision may have obtained their information from a source they considered trustworthy, and they probably have some investment in their research.

Hence, for healthcare professionals, effective communication begins with empathizing with patients, understanding how they get their information, and allowing them to articulate how they feel about the information and their sources for it.^{7,8} Our decision-making process as human beings is largely driven by an emotional core followed by logical justification, as demonstrated by the works of a Nobel Prize-winning economist, Daniel Kahneman.⁹ Thus, getting to the core of a patient's emotional underpinnings may be a counterintuitive method yet could be a research-based approach on how to gain patients' permission to provide them with accurate medical information, continue to be their influential educators, and generally foster successful relationships.

Most oncologists have not had formal communications training, let alone experienced formal longitudinal coursework providing immersive techniques that have a clear evidence base of its efficacy. Yet such training is a widely recognized unmet need,¹⁰⁻¹² which will likely continue to grow in the face of current changes such as artificial intelligence and anticipated future shortages of healthcare professionals. A 2000 survey by the American Society of Clinical Oncology (ASCO) showed that among oncologists attending ASCO communication sessions, only 4.8% had ever received formal training in the instance of giving bad news,¹³ which is considered a core competency in the field. Results of a 2004 survey of oncology training programs indicate that 31% of such programs addressed communications.¹⁴ This possible discrepancy in supplied communications and perceived training experience highlights the need for more formalized and standardized curricula. Physicians may, as a result, also feel uncomfortable about handling discussions involving strong emotions,



Kimberly Ku, MD

and one study indicates that physicians experience significant stress when disclosing bad news to patients.¹⁵ In a study of physician burnout, oncologists were found to feel the least confident and the most anxious when trying to help patients with emotional issues when such physicians reported lack of training in communication skills.¹⁶ Hence, embracing empathetic communications training has potentially widespread benefits for the healthcare system and its beneficiaries.

The value of communication skills training could be quantified beyond the current training format of observing role models during their training and further honed through randomized prospective clinical trial observation of longitudinal immersion with practice, coaching, real-time feedback, and tracked improvements.¹⁷ Author, poet, playwright, and former president of the Czech Republic, Václav Havel, has been quoted as saying, “Hope is not the conviction that something will turn out well but the certainty that something makes sense, regardless of how it turns out.” Being able to maintain this type of confidence in communications skills and the empathetic intent with which healthcare professionals are naturally inclined to approach human problems is more than just a soft skill or blind optimism. Further dedicated clinical study is required so that communication skills training becomes ubiquitously accepted alongside other hard science training and so that we can see tangible links to the various practical results that we most value, such as clinical outcomes, overall sense of satisfaction among patients and providers, as well as sustainable use of resources, time, and financial and social responsibility.

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Regulatory Actions

Recent therapy approvals, updates, and clinical trial results in the field of hematologic oncology

FDA Approves Blenrep Combo for Relapsed/Refractory Myeloma

By Andrew Moreno

A new indication has been approved by the FDA for belantamab mafodotin-blmf (blenrep) in multiple myeloma (MM), GSK has announced. The approval is specifically for blenrep in combination with bortezomib plus dexamethasone to treat relapsed or refractory disease in adults in whom two or more treatments have already been attempted, including an immunomodulatory agent and a proteasome inhibitor.

Combinations featuring Blenrep for relapsed or refractory MM have already been approved as second-line or later therapy in Brazil, Canada, the EU, Japan, Switzerland, and the UK. In China, Blenrep has received Breakthrough Therapy Designation and Priority Review.

“Today’s FDA approval of Blenrep is another significant milestone, providing potential for superior efficacy, including overall survival, to US patients. There is an urgent need for new and novel therapies, as nearly all patients with multiple myeloma experience relapse and re-treating with the same mechanism of action often leads to suboptimal outcomes,” commented GSK chief scientific officer **Tony Wood** in the company’s announcement.

Blenrep is a monoclonal antibody-drug conjugate based on a monoclonal antibody produced with POTELLIGENT Technology licensed from BioWa Inc. and drug linker technology from Seagen Inc. Evidence supporting the use of Blenrep in MM has grown from the work in the ongoing Driving Excellence in Approaches to Multiple Myeloma (DREAMM) clinical trial program.

The new FDA approval matches the study population of the phase 3 DREAMM-7 trial, data from which had been submitted toward that approval. Among the trial’s findings, patients receiving the Blenrep combination had their mortality risk reduced by 51%, with a hazard ratio (HR) of 0.49, and median progression-free survival of 31.3 months as compared with 10.4 months for patients who received a daratumumab-featuring triplet, with an HR of 0.31. The combination’s safety effects and tolerability in the patients also matched expectations from its component’s safety profiles.

Regarding next steps, further Blenrep combination outcomes data are expected in 2028 from the DREAMM-7, DREAMM-8, and DREAMM-10 trials, and expansion of the enrolled study population. This year, GSK will submit DREAMM program data to the National Comprehensive Cancer Network guidelines. The company is also working closely with the FDA on a Risk Evaluation and Mitigation Strategy (REMS) to facilitate the availability of Blenrep to the public while maintaining safety.

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FDA Speedy Review Signals Confidence in Orca-T for Hematologic Malignancies

By Nichole Tucker

Riding the momentum of strong phase 3 Precision-T results unveiled at the Society of Hematologic Oncology (SOHO) Annual Meeting and 51st Annual Meeting of the European Society for Blood and Marrow Transplantation (EBMT), Orca-T has advanced with FDA acceptance of its biologics license application (BLA) under priority review.¹

In the Precision-T trial (NCT04013685), the primary end point of severe chronic graft-vs-host-disease (cGVHD)-free survival (cGFS) was significantly improved with Orca-T vs allogeneic hematopoietic stem cell transplant (alloHSCT) with tacrolimus and methotrexate. There was also a significant improvement in GVHD-free relapse-free survival (GRFS) with Orca-T compared to the control, according to a poster presentation from **Rawan Faramand, MD**, of Moffitt Cancer Center in Tampa, Florida.^{1,2}

Key results showed that at 1 year, the cGFS rate reached 78% (95% CI, 65.0%-86.6%) among patients in the Orca-T arm, compared with 38.4% (95% CI, 26.2%-50.5%) among those who received alloHSCT (HR, 0.26; 95% CI, 0.14-0.47; log-rank $P < 0.001$). The 1-year incidence of moderate to severe cGVHD was also lower with Orca-T at 12.6% (95% CI, 5.3%-23.1%) versus 44% (95% CI, 31.3%-56.1%) in the control group (HR, 0.19; 95% CI, 0.08-0.43; Gray’s test $P < 0.001$).²

The findings come from a cohort of 187 patients, of whom the study team assigned 93 to receive Orca-T and 94 to the alloHSCT arm. In total, 88 patients in the Orca-T arm and 85 in the alloHSCT arm completed follow-up in Precision-T. Of those assigned, the safety population included 88 from the Orca-T arm and 94 from the alloHSCT arm.

In addition to the key outcomes, Precision-T evaluated 1-year non-relapse mortality, which was 3.4% with Orca-T versus 13% with alloHSCT. The 1-year relapse-free survival was 76% in patients treated with Orca-T versus 74% with alloHSCT.

Safety findings outlined major transfusion toxicities and how they compare between the treatment arms. Among patients treated with Orca-T versus alloHSCT, serious treatment-emergent adverse events (AEs) were observed in 39% versus 56%, respectively. Moreover, the 1-year incidence of grade 3 or higher aGVHD was 6.2% versus 16%. The percentage of patients with cGVHD of any grade was 17% in the Orca-T population compared with 49% in the alloHSCT population.

The safety findings presented at SOHO were similar to those announced at EBMT. Further, no new safety signals emerged with Orca-T. Grade 4 or higher infections, per CTCAE criteria, occurred in 6% of patients treated with Orca-T and 10% of those who received alloHSCT.³

The SOHO poster also noted engraftment and hospitalization rates. Results showed a 13-day median timing of neutrophil engraftment among patients treated with Orca-T compared with 14 days in the alloHSCT group. There was a 17-day median timing of platelet engraftment in the Orca-T arm versus 18 days in the alloHSCT arm. The percentage of patients rehospitalized as a result of an AE was 27% for the Orca-T population versus 46% for the alloHSCT population. No primary graft failure was shown in either treatment arm, and there was only one case of secondary graft failure in the Orca-T arm.²

The FDA has set a target action date of April 6, 2026, for the decision on Orca-T for the treatment of acute myeloid leukemia, acute lymphoblastic leukemia, and myelodysplastic syndromes.

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Brexu-Cel Maintains Strong Efficacy in Relapsed or Refractory Mantle Cell Lymphoma

By Nichole Tucker

Five years after the accelerated FDA approval of the autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, brexucabtagene autoleucel (brexu-cel), clinical trial investigators from the phase 2 ZUMA-2 study have unveiled more evidence to support its continued use as a treatment for patients with relapsed or refractory mantle cell lymphoma (MCL).^{1,2}

“Brexu-cel achieves rapid, durable responses regardless of high-risk markers, supporting earlier use in BTKi [Bruton’s tyrosine kinase inhibitor]-naive MCL. Products enriched with juvenile T cells show deeper, longer remissions due to superior fitness and persistence, underscoring the importance of early referral before prior therapies—especially bendamustine—erode T-cell reserve and impact treatment outcome,” study co-investigator, **Andre H. Goy, MD**, of Hackensack University Medical Center, told *Blood Cancers Today*.

Based on a cohort of 86 patients (cohort 3), brexu-cel achieved a 91% (95% CI, 82.5%-95.9%; $P < 0.0001$) objective response rate (ORR) in patients with BTKi-naive relapsed or refractory MCL, meeting the primary end point of the study. The complete response rate was 73% (95% CI, 62.6%-82.2%), and the partial response rate was 17% (95% CI, 10.1%-27.1%). Three patients had stable disease (3%; 95% CI, 0.7%-9.9%), and 3 had progressive disease (3%; 95% CI, 0.7%-9.9%).

The strong responses to brexu-cel in the overall study population were consistent across key subgroups, including patients with high-risk features. Notably, the *TP53*-mutant MCL subgroup achieved an ORR of 100%. Patients with a high tumor burden at baseline had an ORR of 97%, and those with more than 30% *Ki-67* positivity had an ORR of 95%. ORRs in the group of intermediate-to-high-risk patients and those with prior bendamustine treatment were 89% and 83%, respectively. The median time to first objective response was 1.0 month (range, 0.8-6.0 months).

In terms of the secondary efficacy end points of the study, the estimated duration-of-response rate was 80% at 12 months. The estimated 12-month progression-free

survival and overall survival rates were 75% and 90%, respectively.

“Brexu-cel is highly active in BTKi-naive R/R [relapsed or refractory] MCL, with efficacy largely unaffected by high-risk features such as *TP53* mutations, high *Ki-67*, high s-MIPI [simplified Mantle Cell Lymphoma International Prognostic Index], blastoid morphology, or bulky disease,” Dr. Goy stated.

Grade 3 or higher adverse events (AEs) were common, having occurred in 88% of patients treated with brexu-cel during the study. The most common grade 3 or higher AEs included neutropenia (43%), decreased neutrophil count (42%), and decreased white blood cell count (37%). Ninety-one percent of patients experienced grade 3 or higher cytopenias, which had a median time to onset of 3 days (range, 1-93 days).

Of the high-grade events, it was noted that four were grade 5 in severity. Any-grade cytokine release syndrome (CRS) was observed in 95% of patients, with 6% of patients having grade 3 or higher CRS. A 66% incidence of immune effector cell-associated neurotoxicity syndrome (ICANS) was also observed, and ICANS was grade 3 or higher in 21% of patients.

“These data really show that you don’t have to be treated with and fail a BTK inhibitor to benefit from CAR T-cell therapy. In fact, outcomes were better in patients who had one or two prior lines of therapy compared with those who had three or more, which suggests that candidates for CAR T-cell therapy are probably best served by using it earlier in the course of their disease rather than later,” study co-investigator **Brian T. Hill, MD, PhD**, of the Cleveland Clinic in Ohio and Case Western Reserve University, told *Blood Cancers Today* in an interview.



Andre H. Goy, MD



Brian T. Hill, MD, PhD

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Asciminib Ushers in a New Era in the Quest to End Lifelong Therapy

By Nichole Tucker

Tyrosine kinase inhibitor (TKI) therapy still sits at the center of chronic myeloid leukemia (CML) management. Despite 20 years of research, of which some studies explored other drug classes, TKIs have offered the best efficacy, including extending the lives of patients, according to **Jorge Cortes, MD**.

With patient experience at the forefront, even high efficacy and safety are not enough. More work is needed in CML research.

“We’ve made tremendous progress in CML, but sometimes



Jorge Cortes, MD

it gives the impression that we’re done—and if you’re a patient, there’s no way you can think that we’re done,” said Dr. Cortes, professor, Department of Medicine, Medical College of Georgia, and director, Department of The Graduate School at Augusta University, in an interview with *Blood Cancers Today*.

The biggest draw for patients in CML management is not any specific treatment type. According to Dr. Cortes, it is finding a treatment that ultimately helps patients achieve treatment-free-remission (TFR).

Treatment-free-remission is a somewhat novel concept. Dr. Cortes stated that until recently, only about half of the patients were eligible to consider stopping

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therapy. Of those patients who stop therapy, many must resume because of relapse. These outcomes have been improved upon with asciminib moving up to the frontline setting in 2024 and the drug offering the deepest responses among TKIs, aiding in the journey to TFR.

The FDA-approved use of asciminib upfront is based on results from the phase 3 ASC4FIRST study (NCT04971226).¹

In comparison with other TKIs, asciminib demonstrated a more impressive benefit-risk profile in ASC4FIRST and showed better efficacy and safety/tolerability.² The study included 405 patients, of whom 201 underwent asciminib treatment and 204 received other investigator-selected TKIs, including dasatinib, nilotinib, bosutinib, or the standard of care (SOC), imatinib. All patients were evaluated for efficacy.²

Results from Dr. Cortes showed a 48-week major molecular response rate (MMR) of 67.7% in patients treated with asciminib versus 49.0% in those treated with other TKIs (2-sided $P < 0.001$). The MMR rates for the asciminib arm versus those who received SOC, were 69.3% versus 52.9%, respectively (2-sided $P < 0.001$).

Optimal response at week 12 and 24 were key secondary end points of the study. Results showed that at week 12 and 24, asciminib treatment led to optimal responses in 89.5% and 88.5% of patients, respectively, compared with 70.1% and 63.7% of those treated with other TKIs, respectively. Compared with SOC, asciminib also showed superior outcomes at the 12- and 24-week timepoints (88.1% vs 59.8%; 88.1% vs 52.9%).

“With the introduction of asciminib as a frontline therapy, maybe we’re getting closer to having more patients eligible and hopefully more patients who maintain the response,” said Dr. Cortes.

The rate of grade 3 adverse events (AEs) among patients treated with asciminib was 38.0%, which was lower than with any other TKI. In addition, only 4.5% of patients who received asciminib discontinued treatment. Thirty percent of patients who received asciminib required dose adjustment and/or interruption, but this percentage was still lower, compared with other TKIs used in the study.

Common AEs of special interest during the study included gastrointestinal toxicity,

myelosuppression, hypersensitivity, and hepatotoxicity, and in all cases, asciminib had the lowest occurrence rates (34.5%, 43.0%, 24.0%, and 16.5%, respectively).

According to results from the study presented at the 2024 American Society of Hematology Annual Meeting & Exposition, asciminib has the potential to transform the CML treatment landscape. The only dilemma in the way of this transformation is access to treatment, Dr. Cortes stated.

“We want to make sure that every patient that has CML has access to a tyrosine kinase inhibitor...even having access to imatinib, which is already a very good drug, would be a major advance,” he said.

In addition to access, smart monitoring of patients will go a long way to improving outcomes in CML overall, Dr. Cortes hinted.

“We need to continue working on doing more research and optimizing the tools that we have for treatment, for monitoring, for managing patients so that we can offer the best to our patients,” Dr. Cortes said. “We are developing better tools to identify those patients who have the best chance of stopping therapy, which is something that’s called a digital polymerase chain reaction.”

The future of CML management looks hopeful, with multiple TKIs in the pipeline and ongoing efforts to expand patient access and push forward innovations for patient monitoring.

“We’re not done with CML—not until more patients can live free of therapy,” Dr. Cortes concluded.

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Population Study Finds Significant Care Gaps in AML Readmissions

By Jill Elaine Hughes

Rates of hospital readmissions for patients with acute myeloid leukemia (AML) and the proportion of patients without health insurance highlight that gaps in seamless care delivery remain at the system level, according to a database study presented at the 2025 *American Journal of Hematology, Lymphoma, Leukemia & Myeloma* Congress.

In this study, **Jasneet Randhawa, MD**, and researchers at Hamilton Medical Center, in Dalton, Georgia, evaluated cases of AML as recorded by the 2022 Nationwide Readmissions Database (NRD), part of the Healthcare Cost and Utilization Project of the US Agency for Healthcare Research and Quality. Given the population-level impact of AML (nearly 11,000 associated US deaths annually), the research team determined at study outset that “gaps remain in understanding how hospital- and patient-level factors influence early readmissions.” The research team designed the study to identify statistically significant predictors of 90-day readmission “to help reduce preventable mortality and improve outcomes for patients.” Costs associated with initial index stay and any subsequent inclusion readmissions were also evaluated.

The study researchers reviewed NRD data for patients hospitalized with a diagnosis of AML that occurred between January 2022 and October 2022. All-cause hospital readmission was defined as occurring within 90 days of the initial AML-related hospitalization. “Using survey-weighted logistic, linear, and Cox regression models, we examined clinical and hospital-level characteristics and identified predictors of 90-day readmission,” the authors reported.

Initial inclusion criteria identified 23,182 index (AML-related) hospital



Jasneet Randhawa, MD

admissions, and 9,965 patients were readmitted within 90 days. A total of 2,353 deaths occurred during the initial AML hospital stays. Average length of stay during initial stay was 15.6 days, with mean total charges of \$236,529 and mean costs of \$61,678. Among readmitted patients, average readmission stay was 17.5 days; mean readmission charges were \$256,280, and mean readmission costs were \$66,604. Of note, the readmission cohort accounted for significant total healthcare utilization: 174,314 hospital days, \$2.51 billion in charges, and \$652 million in costs.

The study showed that patients treated at medium- or large-sized hospitals and those discharged from urban teaching hospitals had higher rates of readmission. Government (nonfederal) hospitals had lower readmission rates compared with private hospitals. Medicaid and uninsured/self-pay patients had higher readmission rates than patients with Medicare. Higher readmission risk signals included gout (adjusted hazard ratio [aHR], 1.37), HIV infection (aHR, 2.99), neutropenia (aHR, 1.16), and tumor lysis syndrome (aHR, 1.27). Common non-cancer-related readmission causes included sepsis, pancytopenia, and COVID-19.

According to the researchers, addressing underinsurance could help reduce preventable readmissions and improve outcomes, but they do not provide any indication that a relevant follow-up study will be conducted.

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World Trade Center Dust Tied to Genetic Mutations Behind Blood Cancers

By Lauren Evoy Davis

A study from the Montefiore Einstein Comprehensive Cancer Center (MECCC) found that blood-forming cells may link to an increased risk of leukemia and other hematologic malignancies related to the collapse of the World Trade Center (WTC) twin towers in New York City on September 11, 2001.¹ The authors recently published these findings in *Cancer Discovery*, a journal of the American Association for Cancer Research.

This collapse of the twin towers created large amounts of airborne dust, filled with toxic substances and carcinogens. Approximately 400,000 people—firefighters, police officers, area workers, and nearby residents—inhaled dust particles, asbestos, and ash for months.

Using blood samples from approximately 1,000 first responders exposed to particles of the WTC site, the MECCC scientists compared them to a control group between December 2013 and October 2015. The control group included 255 firefighters who were not on the site on September 11 and 198 who were not exposed.

Researchers from MECCC observed higher rates of cancers, heart issues, and other health problems in people living and working near the twin towers following the collapse, compared to the rest of the country, but they hadn't yet looked specifically for the connection between the debris and blood cancers. People exposed to the WTC debris had a higher prevalence of clonal hematopoiesis (CH), which occurs when hematopoietic stem cells develop the same genetic mutations, which can lead to cancer. First responders to the WTC

collapse who had CH were six times more likely (3.7% vs 0.6%, OR=5.73) to develop leukemia than people who did not have this genetic mutation.

CH is associated with the aging process in healthy individuals. The research team noted that first responders younger than age 60 had higher levels of CH, which they attribute to exposure to WTC dust and suggest may accelerate aging.

In mouse models, researchers tested dust collected from the site and noted high levels of the protein IL1RAP, which was very similar to the high CH levels in the first responders. **Divij Verma, PhD**, a Research Assistant Professor in the Department of Oncology at the Albert Einstein College of Medicine, and colleagues identified the inflammation sensor IL1RAP as a therapeutic target in CH, highlighting this as a novel approach to potentially treat people in the future.²

“Our work has implications for people exposed to wildfires, air pollution, military burn pits, and many other exposures,” said Dr. Verma in a news release. “By screening toxin-exposed populations for CH, we could identify people at risk for blood cancers and then potentially treat or even prevent those cancers by targeting IL1RAP”

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Highlights from the **2025 SOCIETY FOR IMMUNOTHERAPY OF CANCER ANNUAL MEETING NOVEMBER 5–9, 2025 IN NATIONAL HARBOR, MARYLAND.**



Novel CD19 CAR T-Cell Therapy Shows Promise in CLL and Follicular Lymphoma

By *Melissa Badamo*

A novel, next-generation CD19 chimeric antigen receptor (CAR) T-cell therapy, JAK-STAT CAR-T, was determined to be safe with promising clinical activity for patients with relapsed or refractory CD19+ follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL) in a small phase 1/b study.¹

Initial results were presented at the 2025 Society for Immunotherapy of Cancer Annual Meeting by **Marcus Butler, MD**, of the Princess Margaret Cancer Centre in Toronto, Canada.

JAK-STAT CAR-T is unique compared with other CAR T-cell therapies because it incorporates signal 3,¹ which is required for optimal T-cell activation.²

“The incorporation of JAK-STAT signaling may correct dysfunctional T cell signaling, which may be an impediment for clinical utility in the autologous setting for diseases like CLL,” Dr. Butler told *Blood Cancers Today*.

To investigate the safety of the in-house–manufactured JAK-STAT CAR T cells, four patients received CAR T-cell infusions at different dose levels. Three patients (2 with FL and 1 with CLL) received 3×10^5 /kg JAK-STAT CAR T cells, and one patient with CLL received 1×10^6 /kg JAK-STAT CAR T cells.¹

One patient experienced grade 3 anemia, and all four patients experienced grade 4 neutropenia.² These hematologic complications were expected, the

researchers noted, and no other severe adverse events or cytokine release syndrome were observed.¹

The investigators also gathered efficacy data from all four patients to assess the clinical activity of the novel treatment. Two patients responded to treatment with successful CAR T-cell engraftment: one patient with FL experienced a complete metabolic response for 9 months with the 3×10^5 /kg-dose level, and one patient with CLL achieved measurable residual disease negativity as determined by flow cytometry at the 1×10^6 /kg-dose level.¹ As for the other two patients, the patient with FL achieved a partial response, but the patient with CLL had progressive disease.² Both were treated at the 3×10^5 /kg-dose level.

A third dose level of 3×10^6 /kg will also be explored if no dose-limiting toxicities are observed with the 1×10^6 /kg-dose in the completed study.

“With these early results in hand, we are moving forward to complete the dose escalation and we are planning a cohort expansion for patients with CLL and produce other assets for targeting solid tumors,” Dr. Butler told *Blood Cancers Today*. “If the lack of significant toxicity is observed, this agent may be ideal for tackling other non-malignant indications such as autoimmunity.”



Marcus Butler, MD

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Investigation Paints Picture of Second Malignancies After CAR T-Cell Therapy for Myeloma, Leukemia, and Lymphoma

By Andrew Moreno

In recipients of chimeric antigen receptor (CAR) T-cell therapy (CAR-T) for cancer, second primary malignancies (SPMs) can manifest after treatment. Researchers from Shenzhen University General Hospital in Guangdong, China, performed a systematic review and meta-analysis to assess the prevalence and types of these malignancies in patients treated with CAR T-cell therapy for myeloma, leukemia, or lymphoma. They presented their findings at the 2025 Society for Immunotherapy of Cancer Annual Meeting held in National Harbor, Maryland.

“This study indicates SPM is a clinically relevant long-term adverse event requiring vigilance in CAR-T recipients. The incidence warrants close monitoring,” the investigators wrote.

Delving into four clinical databases, the investigators located 25 clinical trials and 13 real-world studies that were relevant to their search. These studies had a combined population of 15,244 enrolled patients, among whom 640 cases of SPM were found. The patients had a median follow-up of 22.9 months.

The investigators applied a random-effects model for their analysis and

found an overall incidence rate of 4.2% for SPMs in the combined patient population. Their subtype analysis found that the most common type of SPM was hematologic, with a prevalence of 35.9%, most often in the form of acute myeloid leukemia or myelodysplastic syndrome. The next most common SPM types were solid tumors and nonmelanoma skin cancer, with prevalences of 18.4% and 13.8%, respectively.

The researchers noted that more studies are needed to clarify the pathogenesis and risk factors for SPMs in this patient population. However, they determined from their meta-regression analysis that patients' bridging therapies, duration of follow-up, prior treatment lines received, and lymphodepleting chemotherapy regimens were independent risk factors for these malignancies at the study level. They also observed variance in the distribution of malignancies by disease type and CAR T-cell product received.

Reference

Zhang H, et al. 2025 Society for Immunotherapy of Cancer Annual Meeting. Abstract 389.

Off-the-Shelf CAR NKT Therapy Yields Early Responses in Relapsed or Refractory NHL and ALL

By Nichole Tucker

In patients with relapsed or refractory non-Hodgkin's lymphoma (NHL) and acute lymphoblastic leukemia (ALL), the use of allogenic chimeric antigen receptor (CAR) natural killer T (NKT) cells may induce objective responses and appear tolerable, according to results from the phase 1 MULTIPRAT study.

Findings from the interim analysis of the study (NCT00840853) were presented by **Amy Courtney, PhD**, during the 2025 Society for Immunotherapy of Cancer Annual Meeting in National Harbor, Maryland. The positive early efficacy notably occurred in patients whose disease relapsed after multiple salvage therapies, including commercially available CAR T-cell therapies.

The study investigators used NKT cells from an investigational bank of healthy donors. The NKT cells co-expressed CD19, interleukin 15, and short hairpin RNA and targeted β_2 -microglobulin and CD74, helping to suppress human leukocyte antigen (HLA) class I and II expression. Patients in the study received escalating doses of NKT cells starting at 1×10^7 (dose level 1). This dose was followed by 3×10^7 (dose level 2) and 1×10^8 CAR-NKT cells/m² (dose level 3).

At the time of the interim analysis, nine patients with NHL had received infusions at all three dose levels, and three patients with ALL had received infusions at dose level 1. Within 4 to 6 weeks of infusion, partial responses were induced in four of the nine patients with NHL. Two of the partial responses in the patients with NHL became complete responses (CRs) within 3 months. Among patients with ALL, two of three achieved an objective response.

Peripheral blood tests revealed CAR-NKT expansion in one patient with NHL who received dose level 2 and two patients with NHL treated at dose level 3. In the patients with NHL treated at dose level 3, the expansion peaked a week after infusion. Moreover, biopsy specimens of tumor tissue obtained from two patients in the NHL cohort showed CAR-NKTs up to 5 weeks after infusion. In



Amy Courtney, PhD

one patient from the NHL cohort who had a CR, the investigators noted a 2,000-fold expansion event in recipient NKTs, which peaked 6 weeks after infusion but remained heightened through the 12-week mark.

The safety findings showed no dose-limiting toxicities related to CAR NKTs. Two occurrences of low-grade cytokine release syndrome and one case of grade 3 neurotoxicity were observed. All toxicities were resolved.

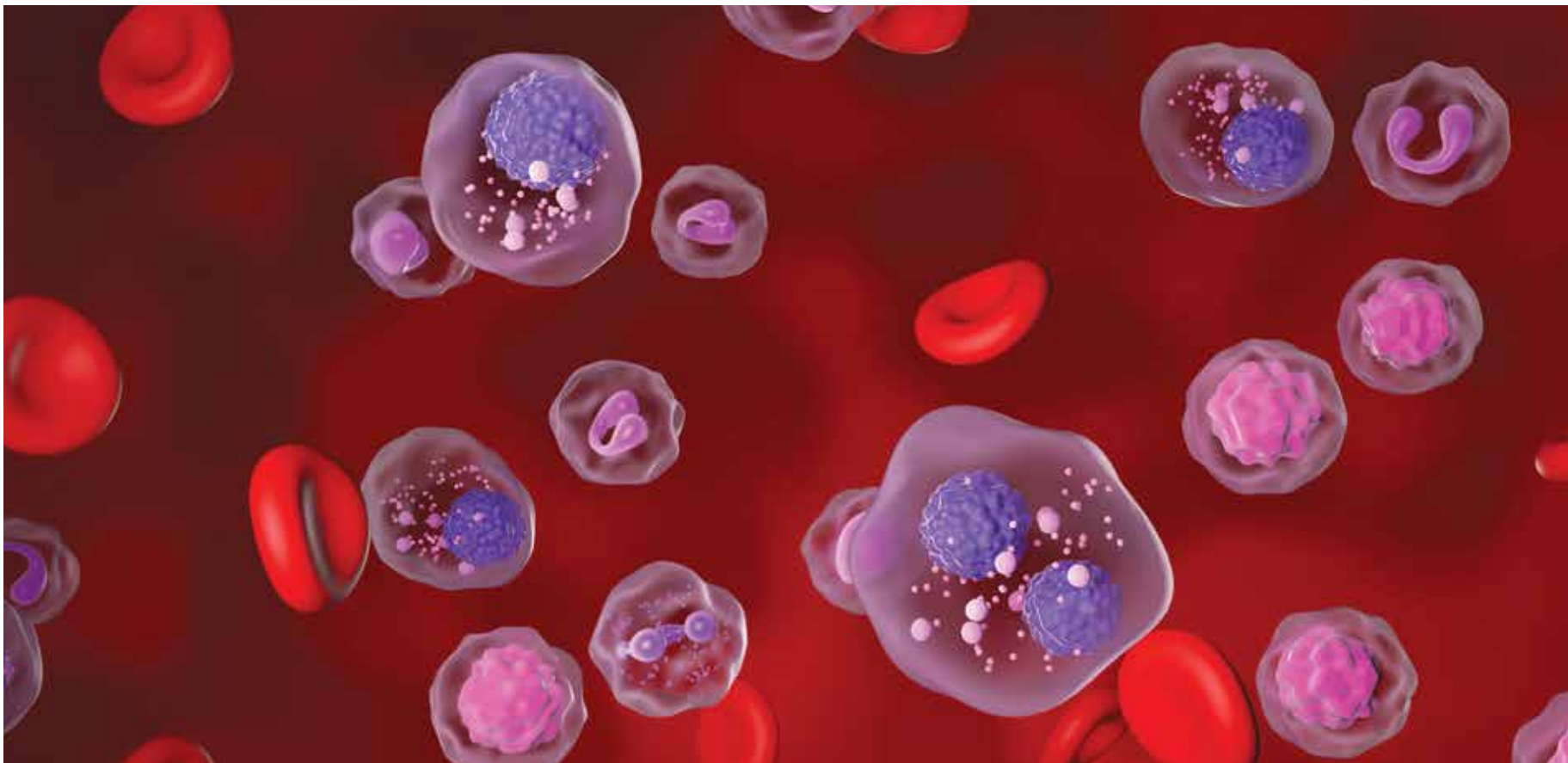
Based on these early results, NKT therapies are encouraging options for off-the-shelf cancer immunotherapy, according to the study investigators.

Reference

Courtney A, et al. *J Immunother Cancer*. 2025;13;suppl 2:553. https://jtc.bmj.com/content/13/Suppl_2/A632

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BAFF Ligand–Based CAR T-Cell Agent for Refractory DLBCL, MCL, and Multiple Myeloma in Development

By Andrew Moreno

A novel autologous B-cell activating factor (BAFF) ligand–based chimeric antigen receptor (CAR) T-cell agent, targeting the BAFFR/BR3, TACI, and BCMA BAFF receptors, is in development for treatment of lymphomas and myelomas that have withstood BCMA- and CD19-targeting CAR T-cell therapies.

This agent, designated LMY-920, is being evaluated in an ongoing study. Favorable interim efficacy and safety data from this study were presented at the 2025 Society for Immunotherapy of Cancer Annual Meeting held in National Harbor, Maryland.

“LMY-920 is very novel in that the CAR-T construct uses a ligand to bind to receptors in the surface of the cell, which is



Paolo Caimi, MD

different than most of the available CAR-T constructs,” first author **Paolo Caimi, MD**, of the Cleveland Clinic Taussig Cancer Center in Ohio, told *Blood Cancers Today*.

These data were drawn from a cohort of five patients. Two patients had diffuse large B-cell lymphoma (DLBCL), two patients had mantle cell lymphoma (MCL), and a fifth patient had multiple myeloma with plasma cell leukemia also present.

Each of the enrolled patients had disease that withstood two to four prior treatment interventions. The investigators highlighted one patient with DLBCL as having undergone prior CD19-targeting CAR T-cell therapy and CD20-targeting bispecific antibody therapy, with loss of lymphoma cell CD19 and CD20 antigens.

All five patients received LMY-920 CAR T-cells at $1-2 \times 10^6$ cells/kg, manufactured using a novel BAFF-CAR transposon construct and administered intravenously. For dosing, the cells were administered following 3+3 escalation from $1-8 \times 10^6$ cells/kg, and no dose-limiting toxicities have been observed in the patients.

The investigators reported interim efficacy results. Both patients with DLBCL have attained a complete response, the disease in both patients with MCL remained stable, and the patient with multiple myeloma had a partial response.

Regarding safety findings, all patients experienced grade 1 or 2 fatigue. In all patients grade 3 or higher severity hematologic toxicity was observed, although in each patient the toxicity had resolved by the 28th day of the trial. There were no instances of immune effector cell–associated neurotoxicity syndrome, but two patients had fever linked to grade 1 cytokine release syndrome.

The investigators noted that dose escalation is still underway for the patients in this ongoing trial.

“The study continues, but the early results are encouraging and suggest that a BAFF ligand CAR-T can be used as treatment of B-cell malignancies,” Dr. Caimi told *Blood Cancers Today*.

Reference

Caimi P, et al. 2025 Society for Immunotherapy of Cancer Annual Meeting. Abstract No. 556.



Visit bloodcancerstoday.com, the online home of *Blood Cancers Today*, for more meeting news.



Editor's Picks

In each issue of *Blood Cancers Today*, we will take a closer look at a particular topic in hematologic malignancies. This month, section editor **Nisha Joseph, MD**, associate professor in the Department of Hematology and Medical Oncology at Emory University School of Medicine, highlights recent research in multiple myeloma.

Visit bloodcancerstoday.com to stay up to date on the latest news in each area of hematologic oncology.



Nisha Joseph, MD



Frontline Multiple Myeloma Daratumumab Carries Elevated Safety Risk, Analysis Finds

By Andrew Moreno

In the frontline management of newly diagnosed multiple myeloma, daratumumab-based therapies carry an increased risk of complications compared with standard regimens. This is according to a systematic review and meta-analysis of safety outcomes presented at the European Society for Medical Oncology 2025 Congress, which convened in Berlin, Germany.

At the Congress, lead author **Saad Nasir, MBBS**, of Aga Khan University Hospital in Karachi, Pakistan, presented the review and meta-analysis. The specific material analyzed by his investigator team to compare daratumumab-containing regimens with standard therapies included six phase 2/3 randomized controlled trials sourced from four clinical research databases. These trials had a combined enrolled study population of 3,624 patients.

Regarding manifestations of second primary malignancies, the primary assessment outcome for the investigators, patients who received daratumumab-based regimens had a markedly higher risk compared with controls, with an odds ratio (OR) of 1.43 ($P=0.005$). Specifically, within this result, they found that daratumumab recipients had a greater incidence of nonmelanoma cutaneous cancers with an OR of 1.90 ($P<0.001$), but the two groups had statistically comparable incidences of solid tumors and hematologic malignancies with ORs of 1.19 and 1.33, respectively.

Comparing risk for hematologic toxicities of grade 3 or worse severity, the daratumumab group had more common neutropenia, with a risk ratio (RR) of 1.31 ($P=0.001$), and showed a statistically nonsignificant trend toward increased thrombocytopenia with an RR of 1.35. However, the study team found grade 3 or worse anemia to be less frequent among daratumumab recipients, with this group having an RR of 0.60 ($P=0.01$).

Outside of these malignancies and hematologic toxicity findings, the investigators also determined that daratumumab recipients have a greater risk of infection with an RR of 1.30 ($P<0.001$, $I^2=0\%$).

Reference

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Linvoseltamab-Carfilzomib Shows Strong Results in Tough Myeloma Cases

By Melissa Badamo

Linvoseltamab plus carfilzomib provides deep and durable responses with an expected safety profile in patients with heavily pretreated relapsed or refractory multiple myeloma, according to initial results from the LINKER-MM2 trial.

The results were presented by **Salomon Manier, MD, PhD**, of Lille University Hospital in France, at the 22nd International Myeloma Society Annual Meeting.

The phase 1b study enrolled 23 adult patients (median age, 70 years) who had progressed after three or more lines of therapy, including a proteasome inhibitor. Linvoseltamab was administered first as two step-up doses of 5 mg and 25 mg. Then, patients received one of three full dose levels: 100 mg (DL1; n=12), 150 mg (DL1b; n=6), and 200mg (DL2; n=5). Linvoseltamab was administered once weekly in cycles 1 through 4, then every 2 weeks.

Carfilzomib 20/56 mg/m² was initiated in cycle 1 on days 1, 2, 8, 9, 15, 16, then could be changed to once weekly after the second cycle. Finally, patients received premedication with dexamethasone before and during the first cycle. The median duration of follow-up was 22.3 months for DL1, 13.2 months for DL1b, and 5.6 months for DL2.

The primary end points were dose-limiting toxicities (DLTs) and treatment-emergent adverse events (TEAEs), and the secondary end points were objective response rate (ORR), duration of response (DOR), and progression-free survival (PFS).

Any grade TEAEs occurred in 61%, and grades 3 or 4 TEAEs occurred in 52% of patients. The most common TEAEs were neutropenia, cytokine release syndrome, thrombocytopenia, and diarrhea, with immune effector cell-associated neurotoxicity syndrome occurring in one patient. Most (91%) patients experienced an infection. One dose-limiting toxicity of grade 4 thrombocytopenia in DL1 was fully resolved, allowing the patient to continue treatment at the same dose.

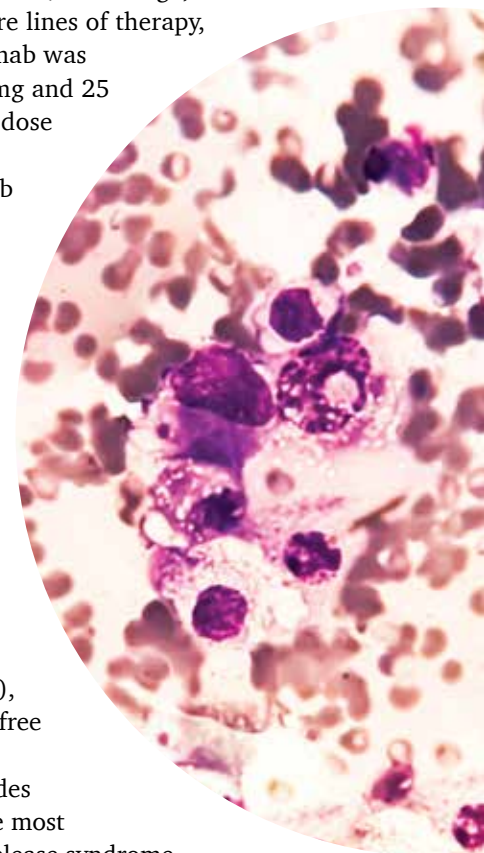
“The safety profile was generally consistent with expectations for this combination based on the known toxicities of each drug,” Dr. Manier told *Blood Cancers Today*.

The combination yielded a high ORR of 91% in DL1, 100% in DL1b, and 80% in DL2, with a DOR rate of 87% (95% CI, 56-97) and a 12-month PFS rate of 83% (95% CI, 55-94). Approximately 71% of measurable residual disease-evaluable patients achieved MRD negativity at 10⁻⁵ sensitivity.

“These encouraging results are being validated in an expansion cohort of the LINKER-MM2 study, and a registrational, randomized phase 3 study testing this combination versus standard of care is planned,” Dr. Manier concluded.

Reference

22nd International Myeloma Society Annual Meeting; September 17-20, 2025; Toronto, Canada. Presentation PA-064.



Cevostamab in Triplet Regimen for Multiple Myeloma: Promising Dose-Expansion Data Presented

By Andrew Moreno

In the phase Ib CAMMA 1 study, the FcRH5/CD3 T-cell-engaging bispecific antibody cevostamab was combined with pomalidomide and dexamethasone as treatment for relapsed or refractory multiple myeloma. Encouraging initial response and safety data from the dose-expansion arm of the study were released at the 22nd International Myeloma Society (IMS) Annual Meeting held in Toronto, Ontario.

The first author of the study was **Hira Mian, MD, MSc**, an associate professor in Oncology at McMaster University in Hamilton, Ontario, and associate editor of *Blood Cancers Today*. At an oral abstracts session of the IMS Annual Meeting, she presented the new CAMMA 1 dose-expansion arm results data.

“We are very excited to see the future development of this compound and hopefully larger trials which will make this accessible to a greater number of patients,” Dr. Mian stated in written remarks forwarded to *Blood Cancers Today*.

The cohort in the dose-expansion arm included 32 patients who had previously received at least one immunomodulatory drug and at least one proteasome inhibitor. They were randomized into two cevostamab dose cohorts of 16 patients each: either 70 mg or 105 mg of cevostamab was administered once every 2 weeks for the first six 28-day cycles and then once every 4 weeks afterward. Both cohorts received pomalidomide 2 mg on days 1 through 21 and dexamethasone 20 mg on days 1, 8, 15, and 22. Patients received the treatment regimen until onset of unacceptable toxicity or disease progression.

The median follow-up in the cevostamab 70-mg cohort was 8.9 months, and in the 105-mg cohort, it was 7.5 months. In the 70-mg cohort, the objective response rate was 93.8%, and the rate of very good partial response or better achieved by patients was 81.3%; in the 105-mg cohort, the respective rates were 62.5% and 62.5%. The 70-mg cohort included 15 patients who responded to treatment, 13 of whom still had a response at cutoff, and in the 105-mg cohort, 10 patients responded to treatment, nine of whom still had response at cutoff.

Regarding safety results, the rate of grade 3 or 4 adverse events was 68.8% in the cevostamab 70-mg cohort and 87.5% in the 105-mg cohort. The rates of grade 3 or 4 neutropenia, anemia, thrombocytopenia, and infections in the 70-mg cohort were 56.3%, 31.3%, 12.5%, and 12.5%, respectively; in the 105-mg cohort, the rates were 62.5%, 12.5%, 37.5%, and 25.0%, respectively. In both cohorts the rate of cytokine release syndrome (CRS) was 81.3%, and in both cohorts 56.3% of CRS instances were grade 1. Two patients died as a result of adverse events unrelated to treatment.

Reference

22nd International Myeloma Society Annual Meeting; September 17-20, 2025; Toronto, Canada. Presentation OA-14.

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HemOnc Happenings

Reporting on recent announcements, awards, and appointments in the hematology/oncology sphere

Dr. Ross Levine Appointed Chief Scientific Officer of Memorial Sloan Kettering Cancer Center After Storied Career

By Sara Karlovitch

Ross Levine, MD, a leading physician-scientist in the field of blood and bone marrow cancers, has been named chief scientific officer (CSO) of the Memorial Sloan Kettering (MSK) Cancer Center in New York. In this role, he will lead strategies for both basic and translational research and oversee the finances and operations of research programs at MSK.



Ross Levine, MD

Dr. Levine will also serve as a strategic partner to the Director of the Sloan Kettering Institute and the Chief Physician Executive to ensure collaboration and research alignment across the organization.

“My goal is to ensure MSK continues to lead in research innovation and in seeing discoveries translated to clinical benefit. We have an incredible group of investigators and initiatives, and my goal is to continue to sharpen our research strategy and ensure we are investing in our talent and ideas,” Dr. Levine told *Blood Cancers Today*.

Dr. Levine comes into the role as the medical research field continues to face uncertainty around

funding. According to Dr. Levine, it is important to successfully communicate research impact and ensure that funding sources are diversified and robust.

“No doubt the biggest challenge right now is the uncertain funding landscape. We need to continue to ensure we have sufficient support for innovative science and our investigators, including from the NIH and other agencies, our supporters, and external partners,” said Dr. Levine.

Dr. Levine’s research at the Ross Levine Lab focuses on JAK-STAT signaling in malignant transformation and the effects of epigenetic modifiers in clonal hematopoiesis and myeloid malignancies such as acute myeloid leukemia. His research team also works to understand the genetic basis for the development of myeloid malignancies by identifying somatic mutations, with the goal of improving therapeutic options for patients.

Dr. Levine joined MSK in 2007, holding several leadership roles over the course of his tenure. In 2016, he served as the inaugural director of the Center for Hematologic Malignancies in 2016 before becoming the first service chief of the Molecular

Cancer Medicine Service of the Human Oncology and Pathogenesis Program. His most recent role was deputy physician-in-chief of Translational Research at Memorial Hospital, where he coordinated efforts to support translational research and oversee activities across several programs and centers.

In recognition of his efforts, Dr. Levine has received the MSK Excellence in Mentoring Award, the Dameshek Prize from the American Society of Hematology, the Pershing Square Sohn Prize for Cancer Research, and more.

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Leading MPN Researchers Honored at ASH Annual Meeting

By Melissa Badamo

Ruben Mesa, MD, of Atrium Health Wake Forest Baptist, and **Radek Skoda, MD**, of the Baylor College of Medicine, received the American Society of Hematology (ASH) Ernest Beutler Lecture and Prize for their roles in advancing the understanding of myeloproliferative neoplasms (MPNs) through Janus kinase (JAK) signaling.¹

Dr. Skoda’s leading research built the framework for developing JAK inhibitors as a therapeutic intervention in patients with MPNs. His research team at the University Hospital Basel in Switzerland discovered that *JAK2* gene mutations lead to *JAK2* protein overactivity in blood stem cells, therefore displacing normal blood cells.¹

Dr. Mesa significantly advanced the development and evaluation of JAK inhibitors in MPNs¹ as the principal investigator of several instrumental clinical trials, including the phase 3 PERSIST-1 and SIMPLIFY-1 trials. The PERSIST-1 trial showed that pacritinib was well tolerated and achieved greater



Ruben Mesa, MD



Radek Skoda, MD

spleen response than best available therapy in patients with myelofibrosis.² SIMPLIFY-1 found that momelotinib reduced transfusion independence in JAK-naïve patients with myelofibrosis and was non-inferior to ruxolitinib in terms of spleen response.³

Dr. Mesa also served as the investigator on the JAKARTA-2 and FREEDOM-2 trials, which established the efficacy and safety of fedratinib as a second-line therapy in patients with myelofibrosis who failed rituximab.^{4,5} In addition, he helped develop the Myeloproliferative Neoplasm Symptom Assessment Form and the Myelofibrosis Symptom Assessment Form as standardized symptom assessment tools in patients with MPNs.¹

“I am deeply honored to be the clinical recipient of this year’s Ernest Beutler Prize for the development of JAK inhibitors flowing from the discovery of the *JAK2* mutation in patients with myeloproliferative neoplasms,” Dr. Mesa told *Blood Cancers Today*. “Although I, and I am sure my co-recipient Dr. Skoda, are honored, we also fully recognize the deep pool of collaborators and team of scientists that drove the progress and impact of JAK inhibition. We mainly celebrate the impact this work has had to decrease the suffering patients with MPN face, and the future advances made possible by this work.”

Dr. Mesa currently serves as president of the Advocate Health Cancer National Service Line,

president of Atrium Health Levine Cancer, and executive director of Atrium Health Wake Forest Baptist Comprehensive Cancer Center. Aside from his senior faculty position at Baylor College of Medicine’s Dan L. Duncan Comprehensive Cancer Center, Dr. Skoda serves as co-chair on the MPN Research Foundation Scientific Advisory Board and professor emeritus of Molecular Medicine at the University of Basel, Switzerland.

Overall, the collective work of Drs. Mesa and Skoda has led to FDA approval of four JAK inhibitors: ruxolitinib, fedratinib, pacritinib, and momelotinib.

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