Incyte

MoA
Efficacy
Safety
L-MIND Study Design
Dosing & Administration

For patients with R/R DLBCL who are not eligible for or refuse ASCT[1]

MINJUVI® + Lenalidomide

right after the first relapse

~ 75% of complete responders were still alive at 5 years[2]

MINJUVI®
tafasitamab

www.minjuvi.ch

MINJUVI® is indicated in combination with lenalidomide followed by MINJUVI® monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least one line of systemic CD20-targeted antibody therapy who are not eligible for autologous stem cell transplantation (ASCT).[1]

R/R DLBCL: relapsed or refractory diffuse large B-cell lymphoma; **ASCT:** autologous stem cell transplantation;

Mechanism of action [1, 4, 6-8]

- Tafasitamab is an Fc-enhanced monoclonal antibody that targets the CD19 antigen expressed on the surface of pre-B and mature B lymphocytes (Figure).
- Upon binding to CD19, tafasitamab mediates B-cell lysis through:
  - Engagement of immune effector cells like natural killer cells, T cells and phagocytes
  - Direct induction of cell death (apoptosis).
- The Fc modification results in enhanced antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis.

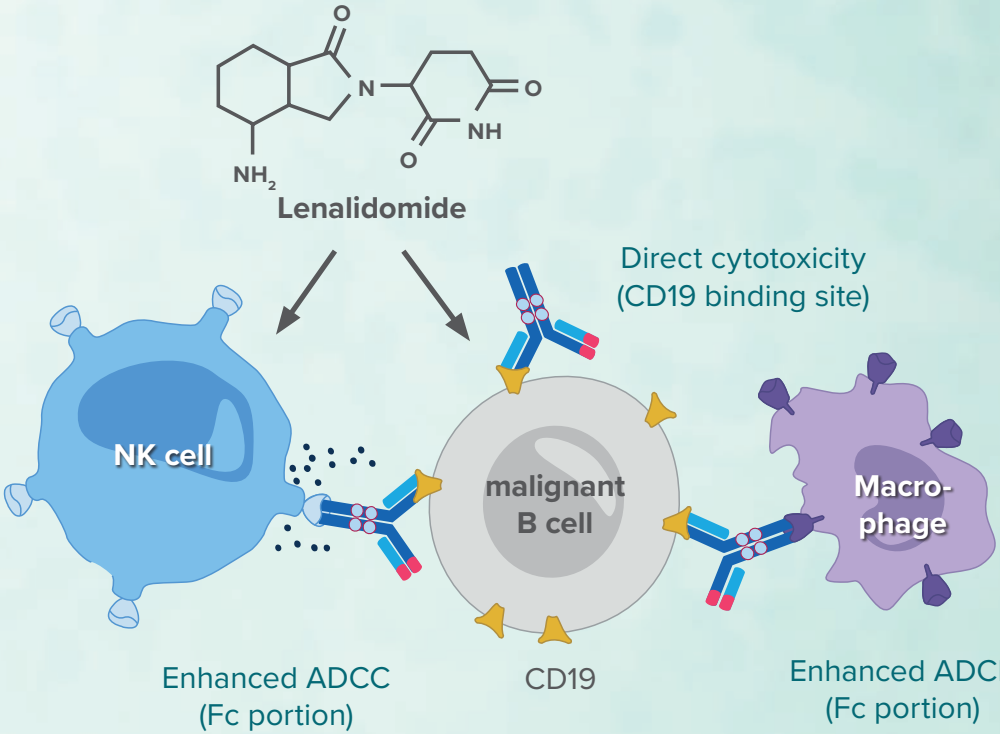
Tafasitamab (Fc-enhanced, anti-CD19 mAb) [4,6-8]

- ADCC ↑
- ADCP ↑
- Direct cell death
- Encouraging single-agent activity in R/R DLBCL and iNHL patients

Lenalidomide [4,6-8]

- T-cell and NK-cell activation/expansion
- Direct cell death
- Well studied as an anti-lymphoma agent, alone or in combination

ADCC: antibody-dependent cellular cytotoxicity; **ADCP:** antibody-dependent cellular phagocytosis; **DLBCL:** diffuse large B-cell lymphoma; **Fc:** crystallisable fragment; **iNHL:** indolent non-Hodgkin lymphoma; **mAb:** monoclonal antibody; **NK:** natural killer; **R/R:** relapsed/refractory.



Adapted from Horton et al. 2008[4]

MINJUVI® tafasitamab

At 5-year follow up in L-MIND:[2]

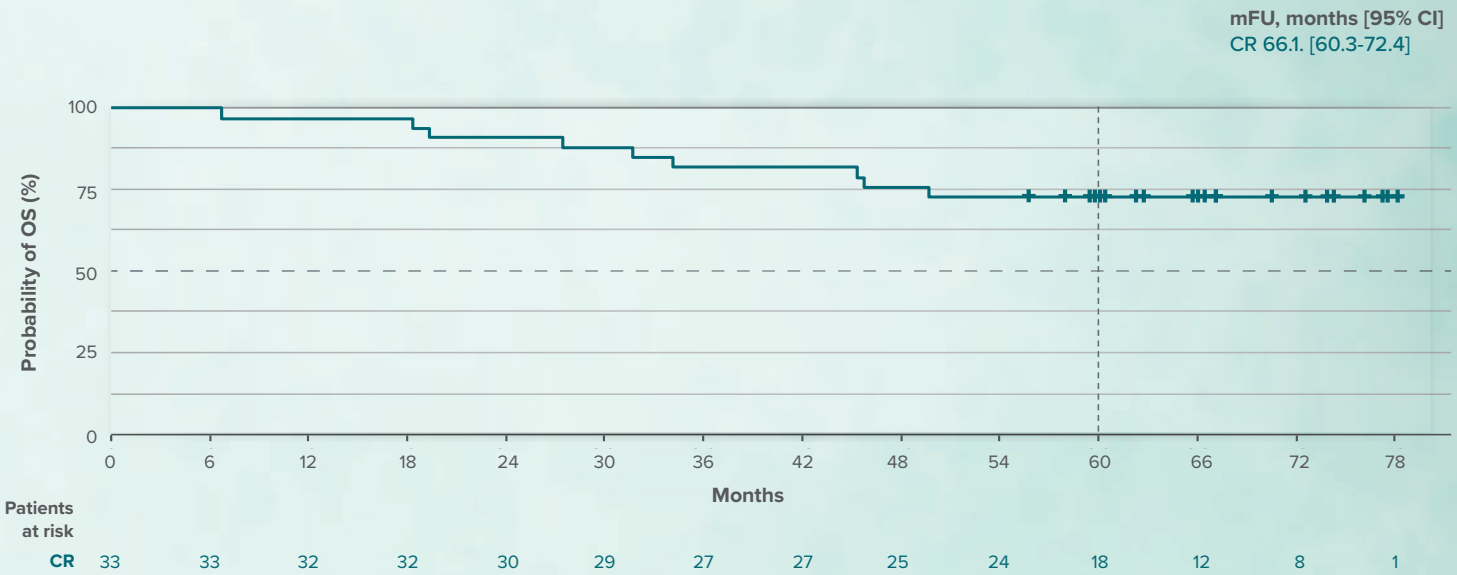
- Over half of patients had a response to treatment
  Best ORR (IRC, FAS): 57.5%
- A majority (71.7%, FAS) of patients who responded to treatment had a complete response

	%, n (n=80, FAS)[2]
Best ORR (IRC)	▶ 57.5% (46/80)
CR	▶ 41.3% (33/80)
CR, as % of responders	▶ 71.7% (33/46)

IRC: independent review committee; **FAS:** full analysis set; **ORR:** objective response rate

Efficacy: 5-year OS by CR[2]

~ 75% of complete responders to MINJUVI + lenalidomide were still alive at 5 years



CI: confidence interval; **CR:** complete remission; **mFU:** median follow-up; **ORR:** objective response rate; **OS:** overall survival

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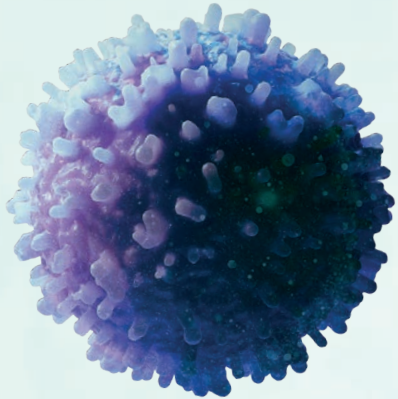
5-year L-MIND data confirmed MINJUVI's rapid response

- Median TTR of two months* (range 1.7–16.8 months) [FAS]

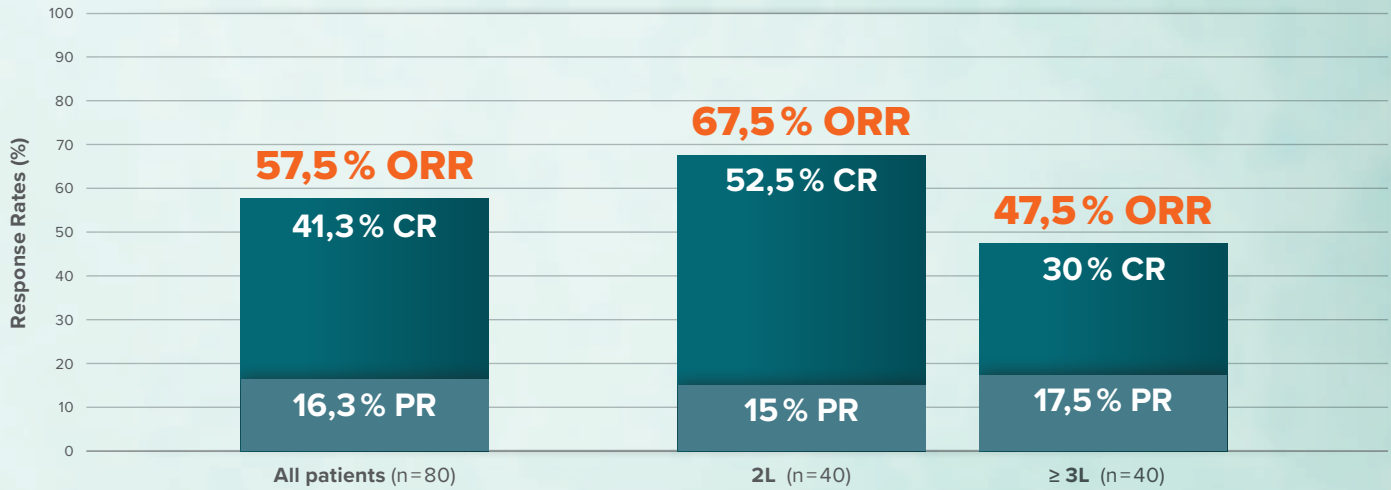
	(n=80, FAS)[2]
mTTR, months (range)	▶ 2.0 (1.7–16.8)



*Timing of the first evaluation of response as per protocol
FAS: full analysis set; **TTR:** time to response

5-year follow-up data in L-MIND confirmed MINJUVI's sustained antitumour responses from 2L for adults with NTE R/R DLBCL[2]

Primary Endpoint: **Objective Response Rate (ORR)**[2, a-c]



Median time to response: **2,1 months (1,7 – 34,7)**[3]
In 2L: **More than 50% CR rate**[2]

a Best objective response rate assessed by an independent review committee. **b** Median follow-up 44 months, data cut-off November 2022.
c n = 80 is from the full analysis set. One patient was not included as he/she only received tafasitamab monotherapy.[2]
CR: complete remission; **NTR:** non-transplant eligible; **PR:** partial remission; **ORR:** objective response rate; **2L:** second line; **3L:** third line

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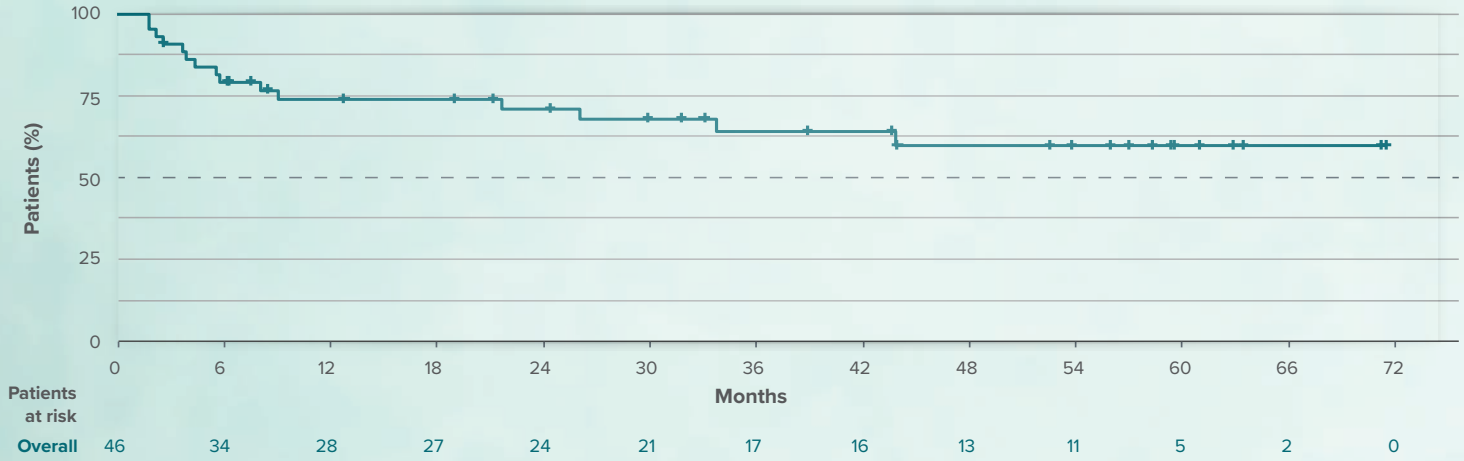
5-year Data: Efficacy Results - DoR[2]

Duration of response: **all patients with PR/CR** and after **best response**[2, a]

mFU, months [95% CI]
Overall 44.0 [29.9, 57.0]

Analysis	Final 5-year data cut-off: 14. Nov 2022		
	Overall	2L	≥ 3L
mDoR, months [95% CI]	NR [33.8, NR]	NR [9.1, NR]	NR [26.1, NR]



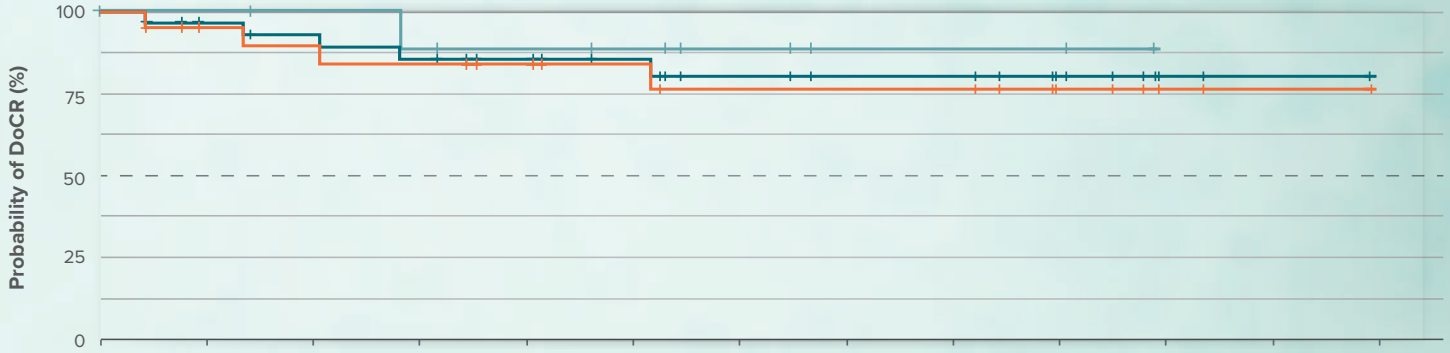
Median DoR was not reached in either subgroup indicating durability of response irrespective of treatment line

a n = 80 represents the full analysis set. One patient was not included as he/she only received tafasitamab monotherapy.[2]
CI: confidence interval; **CR:** complete remission; **mDoR:** median duration of response; **mFU:** median follow-up; **NR:** not reached; **PR:** partial remission; **2L:** second line; **3L:** third line

5-year Data: Efficacy Results - DoCR[2]

Median duration of complete response (mDoCR) was not reached and suggests a plateau after approximately 12 months[2,a]

Analysis	Final 5-year data cut-off: 14. Nov 2022		
	Overall	2L	≥ 3L
mDoCR, months [95% CI]	NR [NR; NR]	NR [31,0; NR]	NR [16,9; NR]



Patients at risk													
Overall	33	27	25	23	20	17	13	11	11	7	2	1	0
2L	21	17	16	15	13	11	9	9	9	5	2	1	0
≥ 3L	12	10	9	8	7	6	4	2	2	2	0	0	0

Median DoCR was not reached in both subgroups underlining long-term efficacy especially in 2L or ≥ 3L

a Median overall follow-up 32.7 months, Data cut-off November 2022
CI: confidence interval; **mDoCR:** median duration of complete respons; **mFU:** median follow-up; **NR:** not reached; **2L:** second line; **3L:** third line

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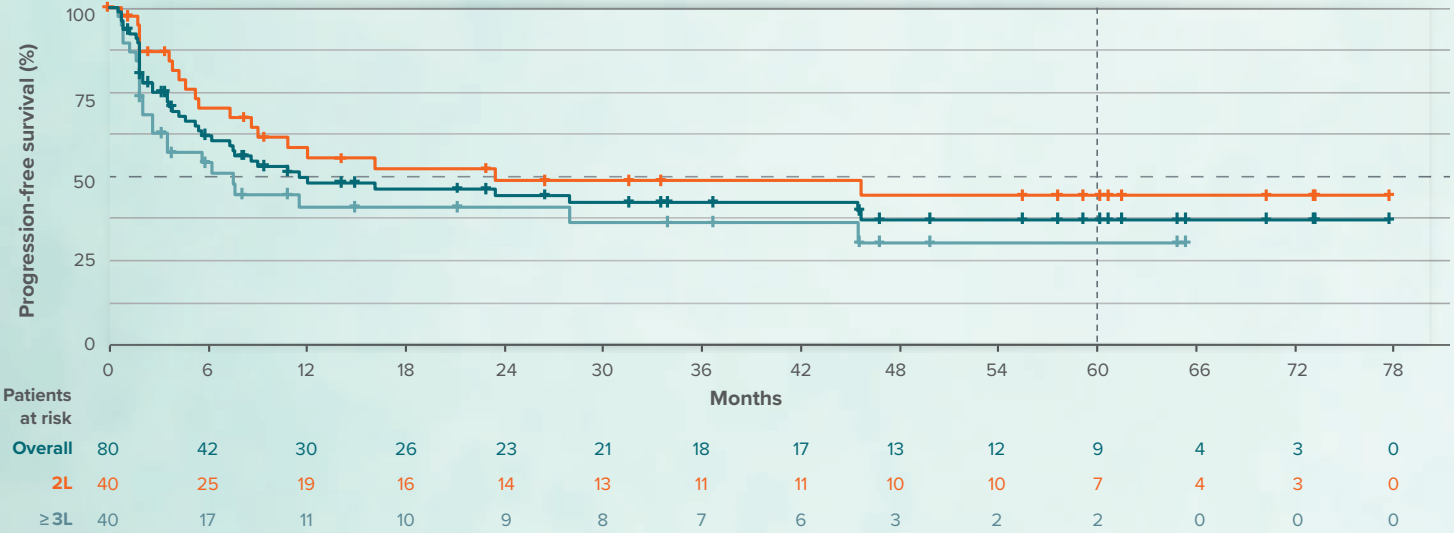
5-year Data: Efficacy Results - PFS[2]

L-MIND subgroup analysis: Median progression-free survival by number of prior therapies [2]

mFU, months [95% CI]
Overall 45.6 [22.9, 57.6]

Analysis	Final 5-year data cut-off: 14. Nov 2022		
	Overall	2L	≥ 3L
mPFS, months [95% CI]	11.6 [5.7, 45.7]	23.5 [7.4, NR]	7.6 [2.7, 45.5]



At 5-years follow-up, almost 2 years of mPFS for patients with 1 prior therapy

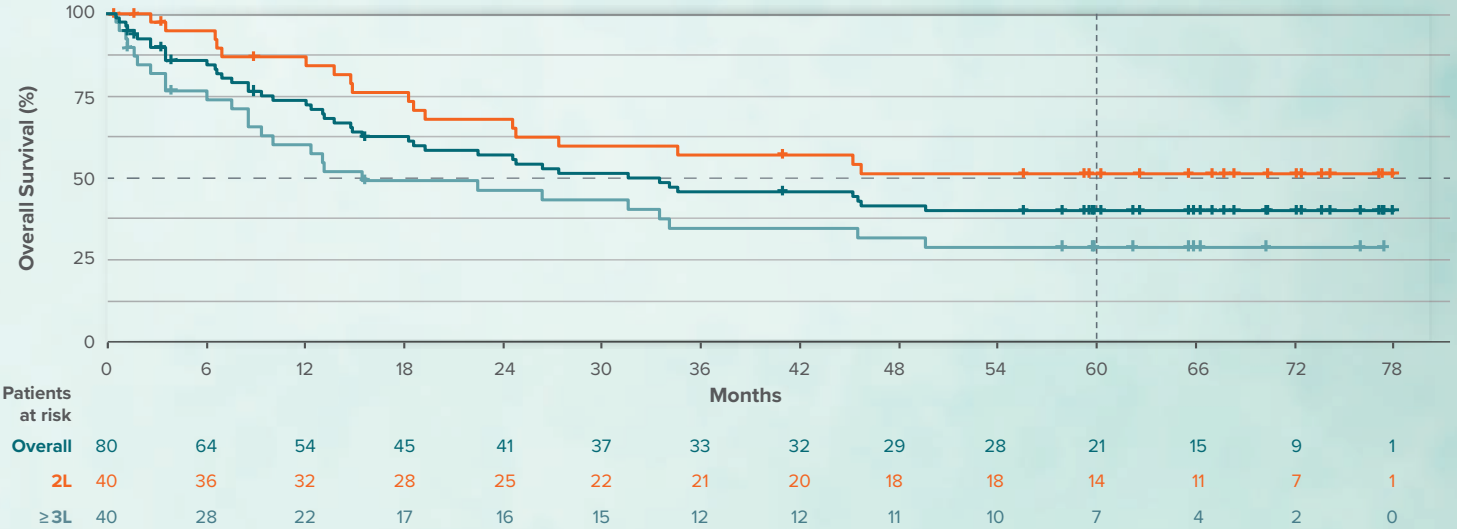
CI: confidence interval; **CR:** complete remission; **mPFS:** progression-free survival; **mFU:** median follow-up; **NR:** not reached; **2L:** second line; **3L:** third line

5-year Data: OS greater with 2L use of MINJUVI®2*

L-MIND subgroup analysis: Median overall survival
by number of prior therapies [2]

mFU, months [95% CI]
Overall 65.6 [59.9, 70.3]

Analysis	Final 5-year data cut-off: 14. Nov 2022		
	Overall	2L	≥ 3L
mOS, months [95% CI]	33.5 [18.3, NR]	NR [24.6, NR]	15.5 [8.6, 45.5]



More than 50% survival probability after 5 years in 2L

*vs. overall (1-3 prior regimens) and/or vs. ≥2 prior lines for R/R NTE DLBCL. Initiation MINJUVI + lenalidomide induction followed by MINJUVI monotherapie

CI: confidence interval; **CR:** complete remission; **mOS:** median overall survival; **mFU:** median follow-up; **NR:** not reached; **2L:** second line; **3L:** third line

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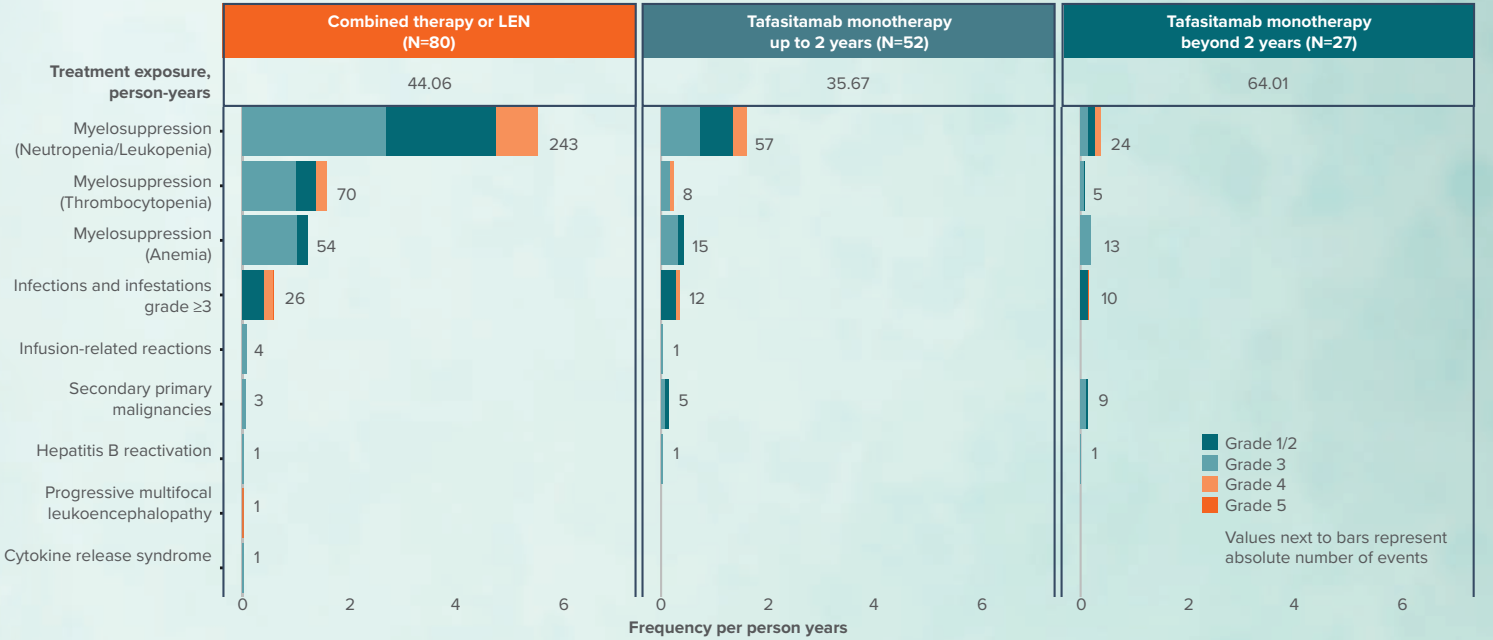
As demonstrated by long-term L-MIND data, MINJUVI® + lenalidomide has an established safety profile consistent with previously reported safety data

Safety results[2]

Exposure-Adjusted Comparison of TEAE Frequency across Treatment Periods

TEAEs of interest:



Low incidence of infusion-related reactions and grade ≥3 infections and infestations

TEAE frequency decreased on transition to MINJUVI® monotherapy – with further decreases beyond 2 years of treatment

LEN: lenalidomide. **TEAE:** treatment-emergent adverse event.

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Study and patient population

L-MIND evaluated the efficacy and safety of MINJUVI® + lenalidomide followed by MINJUVI® monotherapy in adults with NTE R/R DLBCL

- Median patient age was 72 years (range 41–86 years, FAS)[2]
- Half of patients were in 2L (FAS, n=40/80)[2]
- MINJUVI® + lenalidomide is an option particularly where CAR-T is inappropriate[3]

CAR-T: chimeric antigen receptor-T-cells; **FAS:** full analysis set; **NTE:** non-transpant eliglible; **R/R DLBCL:** relapsed or refractory diffuse large B-cell lymphoma

L-MIND: Design of the registration study[1,2]

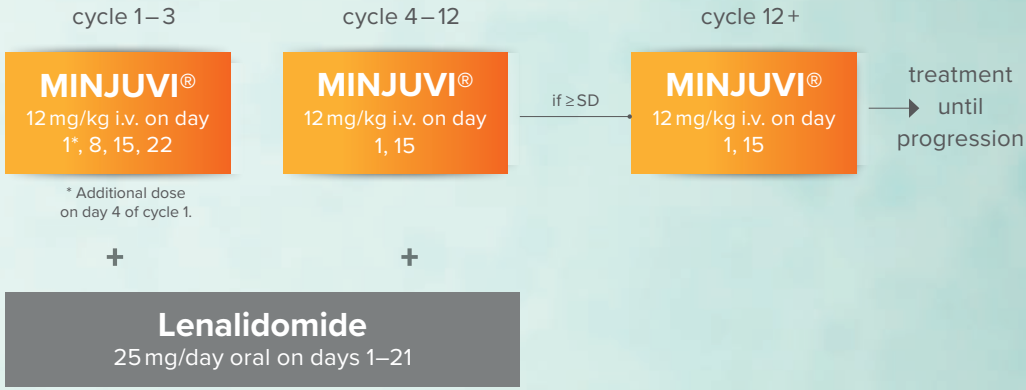
Open-label, multicentric, single-arm Phase II study with **n=81 participants**

Selected Inclusion Criteria

- R/R DLBCL
- Ineligible for ASCT
- Refused ASCT
- 1–3 prior therapies
- ECOG PS 0–2

Selected Exclusion Criteria

- CNS involvement
- Prior CD19 therapy
- Prior iMID therapy



Primary Endpoint

- Objective Response Rate (ORR)

Selected Secondary Endpoints

- Duration of response (DoR)
- Overall survival (OS)
- Safety

ASCT: autologous stem cell transplantation; **ECOG PS:** Eastern Cooperative Oncology Group Performance Status; **R/R DLBCL:** relapsed or refractory diffuse large B-cell lymphoma; **SD:** stable disease; **iMID:** Immunomodulatory imide drug

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Patient characteristics [1,2]

Selected patient characteristics

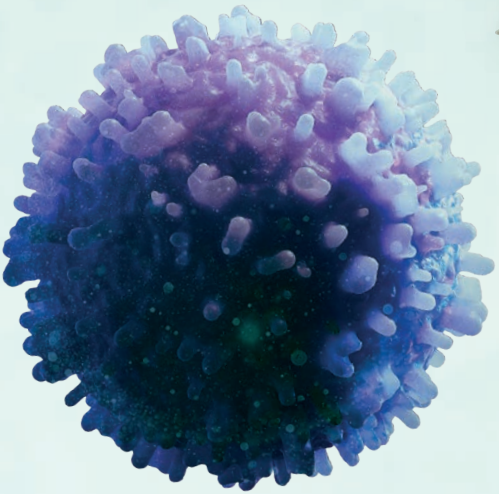
Median age (years)[1]	Median	72 (Range: 41–86)
Gender (%)[1]	Male	54
	Female	46
ECOG PS (%)[1]	0–1	91
Risk (IPI-Score) (%)[2]	0–2	50
	3–5	50
Ann Arbor Stage (%)[2]	I–II	25
	III–IV	75
Elevated LDH (%)[2]	Yes	55
Cell of origin (IHC; %)[2]	GCB	48
	Non-GCB	28
	unknown	25

GCB: germinal center B; **IHC:** immunohistochemistry; **IPI:** international prognosis index;
LDH: lactate dehydrogenase; **ECOG PS:** Eastern Cooperative Oncology Group Performance Status

Prior therapies

Number of prior therapies[1]	Median	2
(%)	1	49
(%)	2	43
(%)	3	6
Primary refractory (%)[1]	Yes	19
Refractory to last therapy (%)[1]	Yes	44
Refractory to rituximab (%)[1]	Yes	42
Prior ASCT (%)[1]	Yes	11
Prior CD20-containing regimen (%)[1]	Yes	100

ASCT: autologous stem cell transplantation



Dosing schedule[1]

Cycle 1

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
MINJUVI® 12 mg/kg	■			■				■							■							■						
Lenalidomide 25 mg/day	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●							

Cycles 2 and 3

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
MINJUVI® 12 mg/kg	■							■							■							■						
Lenalidomide 25 mg/day	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●							

Cycles 4 to 12

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
MINJUVI® 12 mg/kg	■														■													
Lenalidomide 25 mg/day	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●							

After cycle 12

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
MINJUVI® 12 mg/kg	■														■													

After a maximum of 12 cycles of combination therapy, MINJUVI® should be continued as monotherapy until progression or unacceptable toxicity.[1]

MINJUVI® tafasitamab

Administration details[1]

MINJUVI® must be administered by healthcare professionals experienced in treating cancer patients.

First infusion

- Infusion rate in the first 30 minutes: 70 ml/h
- Thereafter, increase rate to complete the infusion within 2,5 hours

Subsequent infusions

- All subsequent infusions should be administered within 1,5–2 hours.

Recommended premedication

Premedication to reduce the risk of infusion-related reactions should be administered 0,2–2 hours before infusion of MINJUVI®.
The premedication is optional if no infusion-related reactions occurred in the first three infusions.

Possible substance groups for premedication:

- Antipyretics (e.g. paracetamol)
- Histamine H1 receptor blockers (e.g. diphenhydramine)
- Histamine H2 receptor blockers (e.g. cimetidine)
- Glucocorticosteroids (e.g. methylprednisolone)

Patient body weight	Number of vials per infusion	Cycle 1	Cycle 2	Cycle 3	Cycle ≥4
		5 infusions	4 infusions	4 infusions	2 infusions
		Number of vials per cycle			
51-66 kg	4	20	16	16	8
67-83 kg	5	25	20	20	10
84-100 kg	6	30	24	24	12

Determine the dose of tafasitamab based on patient weight by multiplying 12 mg with the patient weight (kg). Then calculate the number of tafasitamab vials needed (each vial contains 200 mg tafasitamab).

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Dose modifications in case of adverse reactions[1]

Complete blood count (CBC) should be monitored throughout treatment and before each treatment cycle.

Severity	Dose modifications for infusion-related reactions[1]
Grade 2 (moderate)	▶ Interrupt MINJUVI® infusion immediately and treat signs and symptoms. ▶ Once signs and symptoms resolve or reduce to Grade 1, resume MINJUVI® infusion at no more than 50 % of the rate at which the reaction occurred. If the patient does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to reach the rate at which the reaction occurred.
Grade 3 (severe)	▶ Interrupt MINJUVI® infusion immediately and treat signs and symptoms. ▶ Once signs and symptoms resolve or reduce to Grade 1, resume MINJUVI® infusion at no more than 25 % of the rate at which the reaction occurred. If the patient does not experience further reaction within 1 hour and vital signs are stable, the infusion rate may be increased every 30 minutes as tolerated to a maximum of 50 % of the rate at which the reaction occurred. ▶ If after rechallenge the reaction returns, stop the infusion immediately.
Grade 4 (life-threatening)	▶ Stop the infusion immediately and permanently discontinue MINJUVI®.

Monitor patients for symptoms and signs of progressive multifocal leukoencephalopathy (PML); suspend treatment in case of suspected PML.

Severity	Dose modifications for myelosuppression[1]
Platelet count of less than 50'000/µL	▶ Withhold MINJUVI® and lenalidomide and monitor complete blood count (CBC) weekly until platelet count is 50'000/µL or higher. ▶ Resume MINJUVI® at the same dose and lenalidomide at a reduced dose if platelet count gets back to a value ≥ 50'000/µL. Refer to lenalidomide professional information for dosage modifications.
Neutrophil count of less than 1000/µL for at least 7 days **OR** **Neutrophil count of less than 1000/µL with an increase of body temperature to 38°C or higher** **OR** **Neutrophil count of less than 500/µL**	▶ Withhold MINJUVI® and lenalidomide and monitor CBC weekly until neutrophil count is 1000/µL or higher. ▶ Resume MINJUVI® at the same dose and lenalidomide at a reduced dose. Refer to lenalidomide professional information for dosage modifications.

Neutropenia, including febrile neutropenia, has been reported during treatment with MINJUVI®. Administration of granulocyte colony-stimulating factors (G-CSF) may be considered. Anticipate, evaluate and treat any symptoms or signs of developing infection.

Detailed product information [1,5]

Pharmaceutical form	▶ White to slightly yellowish lyophilised powder. Supplied in single-use 20 ml glass vials containing 200 mg of tafasitamab. Genotoxicity, carcinogenicity or reproductive studies have not been performed. ▶ May be harmful if swallowed, in contact with skin or inhaled.
Excipients	▶ Each vial contains 414,6 mg excipients: Sodium citrate dihydrate (31,6 mg), Citric acid monohydrate (3,7 mg), Trehalose dihydrate (378,3 mg), Polysorbate 20 (1,0 mg)
Storage conditions	▶ MINJUVI® should be stored unopened in its original packaging to protect from light. The carton has the following dimensions: 60 × 75 × 35 mm.
Reconstitution and dilution	▶ Use appropriate aseptic technique for reconstitution and dilution under ambient light. ▶ Reconstitute with 5,0 ml WFI, resulting in a concentration of 40 mg/ml and final density of 1,043 g/l. ▶ To ensure that 5,0 ml, corresponding to 200 mg, can be extracted from the vials after reconstitution, an overfill of 0,4 ml is applied. ▶ The reconstituted solution is diluted for infusion in a 0,9 % sodium chloride infusion bag (250 ml standard).

For stability of the reconstituted and diluted solution refer to the current professional information published on www.swissmedicinfo.ch

Required administration equipment	▶ Administered by IV infusion. ▶ No light protection or filter units are needed. ▶ The Phaseal closed-system transfer device may be used upon a satisfactory risk assessment; MINJUVI® has not been tested in other closed systems. ▶ Compatible with infusion containers made of glass, polypropylene, polyvinylchloride, polyethylene, polyethylene, terephthalate and polyolefin. ▶ Compatible with infusion sets made of polyurethane or polyvinylchloride. ▶ Compatible with 0,2 µm in-line filters made of polyethersulfone or positively charged polyethersulfone or 15 µm mesh filter made of nylon.

IV: intravenous; **WFI:** water for injection.

Pharmacy Manual [5]

Compositions*	Concentration in reconstituted DP, mmol/L	Concentration in reconstituted DP, mg/ml	Nominal amount, mg/vial	Function
Tafasitamab molecular weight: 150 kDa	0,267	40,0	200,0	Active ingredient
Sodium citrate dihydrate molecular weight: 294,10 g/mol	21,5	6,32	31,6	Buffer component
Citric acid monohydrate molecular weight: 210,14 g/mol	3,5	0,74	3,7	Buffer component
Trehalose dihydrate molecular weight: 378,34 g/mol	200	75,67	378,3	Osmolyte, cake former
Polysorbat 20	–	0,20	1,0	Stabiliser, surfactant
Water for injection	–	–	Removed during lyophilisation	Solvent

*Nitrogen gas is used for backfilling (aeration of lyophilisation chamber).
DP: drug product

Storage

- Unopened vials of MINJUVI® must be stored at 2–8 °C (36–46 °F).
- The vials should not be exposed to direct sunlight.
- The shelf life of unopened vials is 4 years.
  The drug may only be used until the date marked „EXP“ on the package.

Overfill

- An overfill of 0,4 ml (target fill of 5,4 ml) equates to 216 mg tafasitamab in each vial.
- After reconstitution, and once the MINJUVI® residue in the reconstitution vial and transfer syringe is compensated for, the amount of tafasitamab transferred into the infusion bag corresponds to 200 mg.
- Owing to machine accuracy, the actual filling volume can range between 5,2 and 5,6 ml, which equates to a range of 208–224 mg tafasitamab in each vial.

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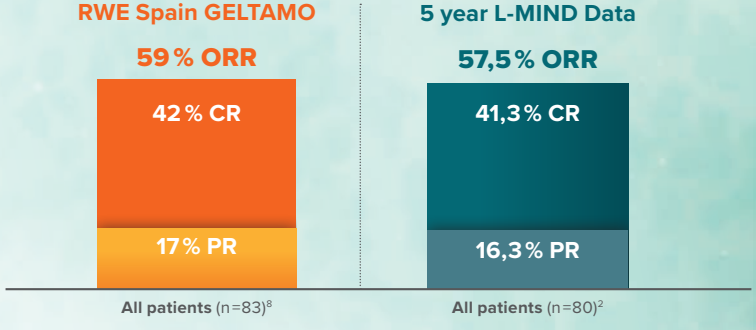
In the Real World Evidence cohort from Spain, Tafa+LEN was found to be effective and generally well tolerated.

Response rates were higher for patients in 2L/3L and higher in relapsed vs refractory patients.[8]



a In the overall population, the CR rate was 52.5%.
2L: second line; **3L:** third line; **CR:** complete remission; **PR:** progressive disease; **ORR:** objective response rate; **RWE:** real world evidence; **Tafa+LEN:** tafasitamab plus lenalidomide

1 MINJUVI Professional Information. See www.swissmedicinfo.ch **2** Duell J et al.,Tafasitamab for patients with relapsed or refractory diffuse large B-cell lymphoma: final 5-year efficacy and safety findings in the phase II L-MIND study; Haematologica. 2024;109(2):553–566. **3** Duell J et al., Long-term outcomes from the phase II L-MIND study of tafasitamab (MOR208) plus lenalidomide in patients with relapsed or refractory diffuse large B-cell lymphoma. Haematologica. 2021; 106(9): 2417 – 26. **4** Horton HM, et al., Potent In vitro and In vivo Activity of an Fc-Engineered Anti-CD19 Monoclonal Antibody against Lymphoma and Leukemia. Cancer Res. 2008;68:8049–57. **5** Data on file, Incyte Corporation. **6** Jurczak W, et al., Phase IIa study of the CD19 antibody MOR208 in patients with relapsed or refractory B-cell non-Hodgkin's lymphoma. Ann Oncol. 2018;29:1266–72. **7** Witzig TE, et al., A comprehensive review of lenalidomide therapy for B-Cell non-Hodgkin lymphoma. Ann Oncol. 2015;26:1667–77. **8** Gutiérrez et al, Tafasitamab plus lenalidomide as salvage therapy in DLBCL: the Spanish Group of Lymphoma (GELTAMO) real world experience; Poster 1203; presented during EHA 2024, June 2024

All references are available upon request.

▼ This medicinal product is subject to additional monitoring. For further information, see professional information MINJUVI on www.swissmedicinfo.ch.

MINJUVI (tafasitamab), 200 mg powder for concentrate for solution for infusion.

I: MINJUVI is indicated in combination with lenalidomide followed by MINJUVI monotherapy for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after at least one line of systemic CD20-targeted antibody therapy who are not eligible for autologous stem cell transplantation (ASCT). **P:** MINJUVI must be administered by a healthcare professional experienced in treatment of cancer patients. The recommended dose is 12 mg of MINJUVI per kg body weight administered as an intravenous infusion. On cycles 1-3: Administer on days 1, 8, 15 and 22 with an additional dose on day 4 of cycle 1. From cycle 4 onwards: Administer on day 1 and 15 of each cycle. In addition, patients should self-administer lenalidomide capsules at the recommended starting dose of 25 mg daily on days 1 to 21 of each 28-day cycle for a maximum of 12 cycles. Dose adjustments due to adverse reactions are needed. **CI:** Hypersensitivity to tafasitamab or any of the excipients. **W/P:** Infusion-related reactions may occur. Patients should be monitored closely throughout infusion. Treatment can cause serious and/or severe myelosuppression. Monitor complete blood counts throughout treatment and prior to administration of each treatment cycle. Withhold MINJUVI based on the severity of the adverse reaction. Fatal and serious infections occurred. Monitor patients for symptoms and signs of progressive multifocal leukoencephalopathy (PML); suspend treatment in case of suspected PML. Administer MINJUVI to patients with an active infection only if the infection is treated appropriately and well controlled. Monitor patients closely for tumor lysis syndrome. QTc prolongation and syncopes have been observed during treatment with MINJUVI. MINJUVI can cause fetal harm. Women of childbearing potential should be advised not to become pregnant during treatment. **IA:** No interaction studies have been performed for tafasitamab. **UE:** The most common adverse reactions (≥ 20%) were infections, asthenia, neutropenia, anaemia, thrombocytopenia and diarrhea. The most common serious adverse reactions (≥ 3 %) were febrile neutropenia and pneumonia. For further information on UE, see www.swissmedicinfo.ch. **Dispensing cat.:** A. **Revision date:** May 2024. **Marketing authorisation holder:** Incyte Biosciences International Sàrl, CH-1110 Morges. MINJUVI and the "triangle" design are (registered) trademarks of Incyte. Refer to www.swissmedicinfo.ch for detailed information.

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