Managing the practicalities of CAR T-cell therapies in patients with R/R MCL: Current considerations and future strategies

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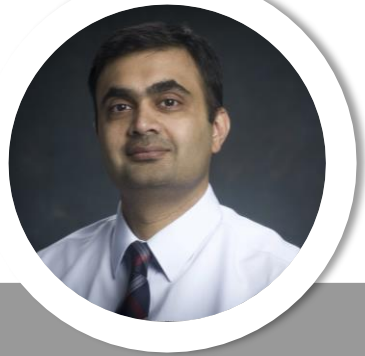

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Agenda

Exploring current treatment strategies for R/R MCL and the role of CAR T-cell therapy

Unravelling the practicalities of CAR T-cell therapies for MCL in the clinic: Focus on toxicities and salvage strategies

Future considerations for optimizing the use of CAR T-cell therapies in patients with MCL

CAR, chimeric antigen receptor; MCL, mantle cell lymphoma; R/R, relapsed or refractory.

Exploring current treatment strategies for R/R MCL and the role of CAR T-cell therapy

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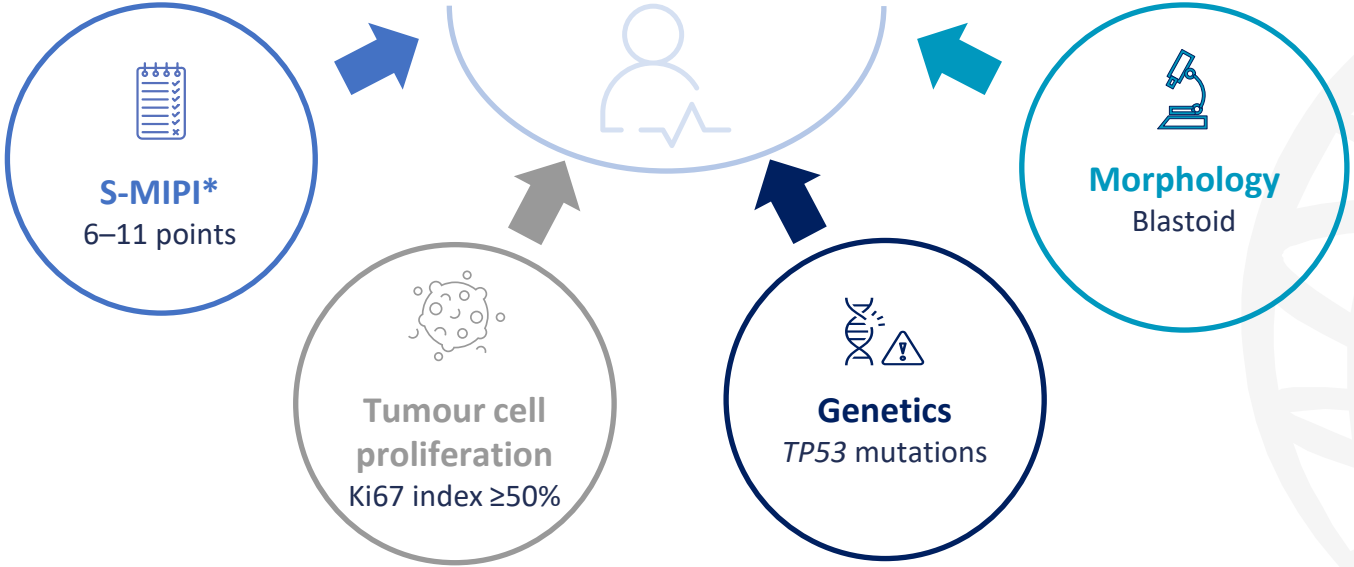
High-risk baseline factors indicating poor prognosis in R/R MCL



- A pooled analysis of patients with R/R MCL treated with ibrutinib monotherapy in the second line found that ~1 in 3 patients have ≥1 poor prognostic feature at baseline
- At follow-up, these patients have an ORR of ~55% and a median PFS of ~6 months

*S-MIPI is based on a sum of scores for age, ECOG PS, LDH and white cell count.
ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; ORR, overall response rate; PFS, progression-free survival; R/R MCL, relapsed or refractory mantle cell lymphoma; S-MIPI, Simplified Mantle Cell Lymphoma International Prognostic Index.
Kumar A, et al. *Am Soc Clin Oncol Educ Book*. 2022:42;614–28.

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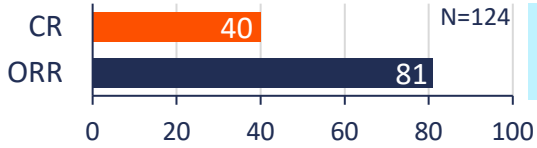
Efficacy of NCCN-preferred agents for R/R MCL*[1]

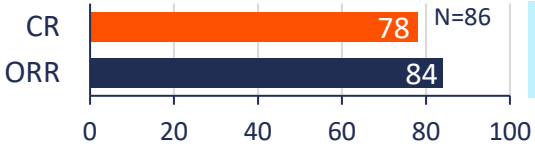
Second line

Acalabrutinib[2,3]



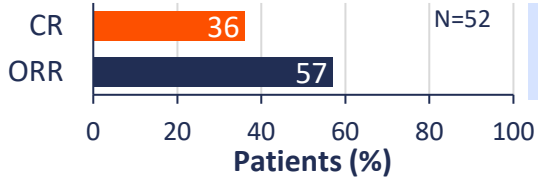
mDoR: 25.7 months
mPFS: 19.5 months

Zanubrutinib[4]



mDoR: NR
mPFS: 33 months

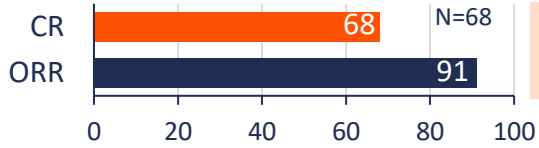
Lenalidomide + rituximab[5]



mDoR: 18.9 months
mPFS: 11.1 months

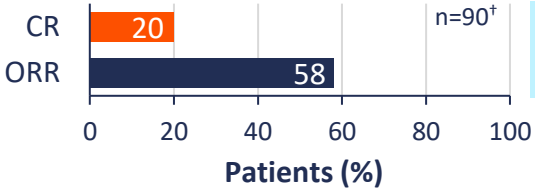
Third line

Brexu-cel[6]



mDoR: 28.2 months
mPFS: 25.8 months

Pirtobrutinib[7]



mDoR: 21.6 months
mPFS: 7.4 months

Direct comparisons between trials should not be made due to differences in trial design. *NCCN guidelines for mantle cell lymphoma. †Sub-group who were pretreated with cBTKi. Brexu-cel, brexucabtagene autoleucel; cBTKi, covalent Bruton tyrosine kinase inhibitor; CR, complete response; DoR, duration of response; m, median; mo, months; NCCN, National Comprehensive Cancer Network; NR, not reached; ORR, overall response rate; PFS, progression-free survival; R/R MCL, relapsed or refractory mantle cell lymphoma.

1. NCCN. B-Cell lymphomas. V6.2023. Available at: www.nccn.org/guidelines/category_1 (accessed 17 November 2023); 2. Wang M, et al. *Lancet*. 2018;391:659–67; 3. Wang M, et al. *Blood*. 2018;132(Suppl. 1):2876; 4. Song Y, et al. *Blood*. 2022;139:3148–58; 5. Wang M, et al. *Lancet Oncol*. 2012;13:716–23; 6. Wang M, et al. *J Clin Oncol.* 2023;41:555–67; 7. Wang ML, et al. *J Clin Oncol*. 2023;41:3988–97.

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Unravelling the practicalities of CAR T-cell therapies for MCL in the clinic: Focus on toxicities and salvage strategies

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Toxicities associated with CAR T-cell therapy and recognized risk factors for them

Specialist centre → **Coordination of care** → **Community care**

Short-term toxicities[1,2]

	Risk factors
CRS	• Increased CAR T-cell expansion • High tumour burden
Neurotoxicity	• Severity of CRS • Disease burden • Baseline inflammation • Neurologic comorbidities
Hematologic	• Severity of CRS/ICANS • High disease burden • Low baseline blood counts

Longer-term toxicities[2]

- Prolonged cytopenia
- Infections
- Secondary malignancies

Patient monitoring is critical for the early recognition of potential toxicities and timely intervention

CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

1. Thompson JA, et al. *J Natl Compr Canc Netw*. 2022;20:387–405;
2. Shaikh S, Shaikh H. 2023. Available at: www.ncbi.nlm.nih.gov/books/NBK592426/ (accessed 17 November 2023).

Future considerations for optimizing the use of CAR T-cell therapies in patients with MCL

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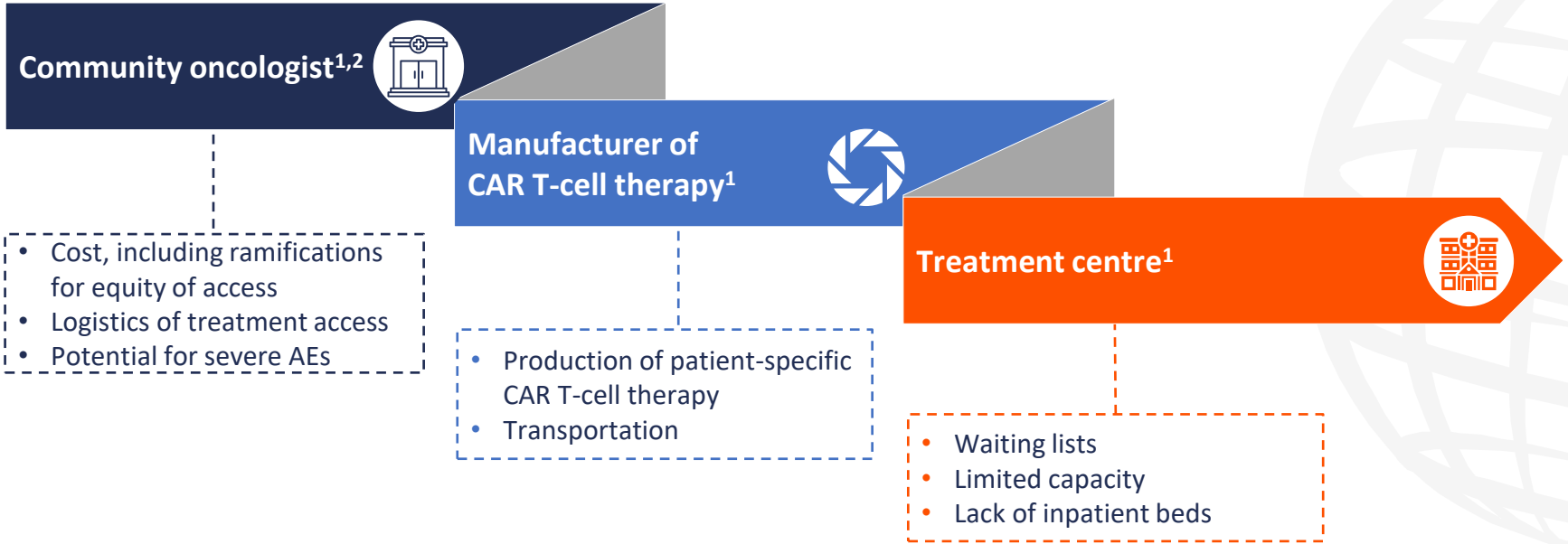
Operational considerations for CAR T-cell therapy



AE, adverse event; CAR, chimeric antigen receptor.

1. Chen AJ, et al. *Value Health*. 2022;25:1344–51; 2. Odstrcil MS, et al. *Blood Rev.* 2023:doi.org/10.1016/j.blre.2023.101136.