Tebentafusp and cytokine release syndrome incidence: A case series of real-world data at two hospitals.

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Context

- Tebentafusp is used for the treatment of patients with advanced *HLA-A*02:01*-positive uveal melanoma.
  - Targets glycoprotein 100 (gp-100) through a high affinity T-cell receptor binding domain and an anti-CD3 T-cell engaging domain, which redirects T-cells to kill tumour cells expressing gp-100.
- Despite the protocol of intra-patient dose escalation to decrease the likelihood of cytokine release syndrome (CRS), in the Phase III trial, 77% of patients experienced CRS Grade 2 (symptomatic CRS) or higher.
- Product information states that during the dose escalation period, patients need to be monitored for signs CRS (for haemodynamic instability) during the infusion and for at least 16 hours after infusion is complete, and appropriate therapy provided if symptomatic CRS occurs.

Aim

- To describe CRS incidence and potential associated risk factors in a real-world setting.

Method

- A retrospective audit was conducted of non-trial patients treated with tebentafusp at 2 Brisbane hospitals between 01/07/2021 and 15/06/2024 by a single prescriber.
- Data collected included burden of disease in the liver, baseline lactate dehydrogenase (LDH), baseline blood pressure (BP), presence and grade of CRS.
- Results were compared to the pivotal Phase III trial data

Findings

- The main results are summarised in Table 1.

Table 1: Characteristics of the patients (n=15) administered tebentafusp

Characteristic	**n (%) of the 15 patients***	
Gender		
Female	8 (53%)	
Male	7 (47%)	
Median age	64~	
CRS G2 or above	7 (47%)^	
G2	5 (33)	
G3	2 (13%)	
Occurrence of reaction		
Dose 1	7 (100%)∞	
Dose 2	0 (0%)	
Dose 3	0 (0%)	
Burden of metastatic disease in the liver (see Fig. 1 & 2, also)	**CRS G1 or below, n=8**	**CRS G2 or above, n=7**
<25%	6 (75%)	2 (28%)
50%	2 (25%)	1 (14%)
>75%	0 (0%)	4 (57%)
Baseline LDH 3x ULN	0 (0%)	4 (57%)
Baseline BP below (120/80)	2 (25%)	2 (29%)

G1= Grade 1, G2= Grade 2, G3= Grade 3, ULN= upper limit of normal.
*6 patients would have been excluded from the Phase III trial for either life expectancy, moderate hepatic impairment, or baseline systemic steroid use.
~Same median age as the pivotal Phase III trial.
^Less incidence of CRS compared to the pivotal Phase III trial (77%).
∞2 patients discontinued tebentafusp post-1st dose due to rapid progression.

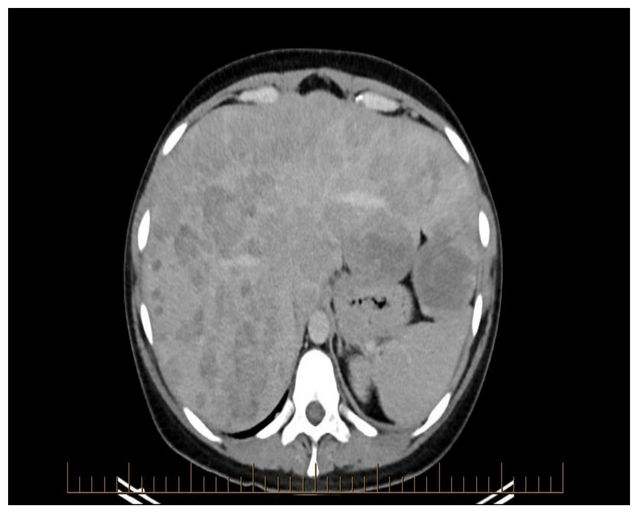

Fig. 1: Patient with high burden of liver disease who experienced CRS Grade 3.

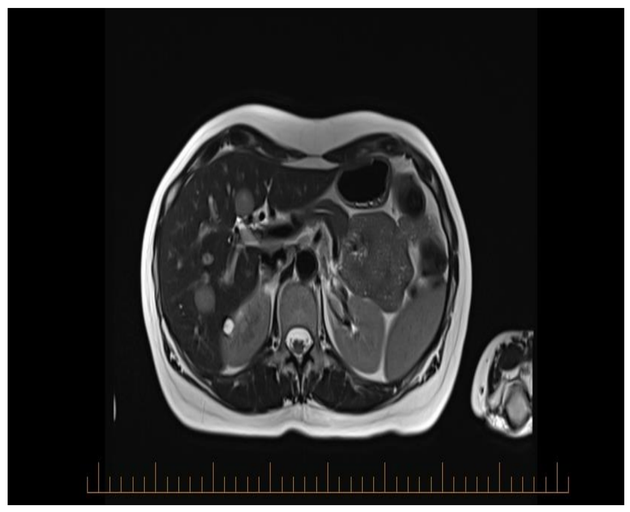

Fig. 2: Patient with low burden of liver disease who experienced CRS Grade 2.

Conclusion

- Burden of liver disease of 50% or more, and/or LDH 3xULN was associated with an increased risk of symptomatic CRS.
- Future research should include a larger real-world patient cohort to identify low-risk and high-risk patients to potentially remove the requirement for low-risk patients to be monitored in the hospital setting during dose escalation.