TEBENTAFUSP IN METASTATIC UVEAL MELANOMA PATIENTS (mUM): VENETO INSTITUTE OF ONCOLOGY EXPERIENCE

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BACKGROUND

- Metastatic uveal melanoma (mUM) is an historically treatment-resistant tumor, whose prognosis is dismal.
- In this setting, the first drug showing a 1-year survival improvement (73% vs 59% in control group) was Tebentafusp (Tebe), a T cell–redirecting bispecific fusion protein, approved by European Medicines Agency in April 2022 (1,2).
- At the moment few real-world data on this agent are available (3,4).

METHODS

We retrospectively collected data concerning HLA A*02:01+ mUM patients (pts) treated with Tebe, between May 2022 and 15h Sep 2023 at our Institution. This is a preliminary descriptive report of clinical characteristics, toxicity information and overall survival (OS) of the whole cohort of pts; moreover for subjects with at least one tumor assessment at data cut-off, resposes according to RECIST 1.1 criteria and PFS were evaluated.

REULTS

- HLA-A*02:01 was found in 12/34 (35%) mUM cases tested. (Fig. 1)
- Eleven (11) HLA-A*02:01+ patients (M:F 6:5, median age 67) were included in this analysis while one was referred to another center

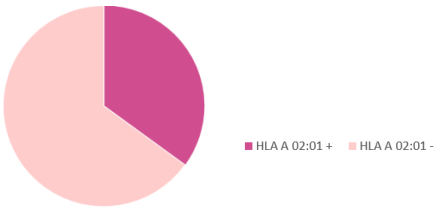

Fig. 1: HLA haplotyping among new mUM diagnoses or progressions referred to our center between May 2022 anSep 2023.

- Study population's baseline characteristics are reported in Tab.1
- Median follow up was 5,4 months.
- All subjects reported drug-related adverse events; cytokine release syndrome (CRS), liver and skin toxicities (vitiligo, rash, dry skin, pruritus) distribution and grade are according to CTACE 5 are reported in Fig. 2. Toxicities decreased in frequency and severity after the dose-escalation phase
- At data cut-off, 8 patients had performed at least one radiologic assessment: efficacy information according to RECIST 1.1 are reported in Fig. 3 .
- Median progression free survival (PFS) was 3.6 months (Fig. 4), overall survival estimation was not possible because of the limited number of events
- The partial responding patient has been receiving treatment for 14 months, experiencing G2 CRS, (early) skin toxicity and, recently, diarrhea responsive to steroids. At baseline intra- and extrahepatic lesions were present, LDH was >2xULN and the largest metastasis diameter was 7 cm (liver, Fig. 5).
- Highest grade (G3) skin toxicity in reported in Fig.6
- Patients with poor performance status at baseline experiencied an early clinical benefit between the first and the fourth administration (after dose esclation phase)(Fig. 7) even if they did not respond according to RECIST.

Patients' baseline characteristics

Age—yr median (range)	67 (57-73)
Sex—no. (%) male female	 6 (55) 5 (45)
Treatment of primary UM—no (%) localized plaque radiation therapy (brachy) Enucleation None	 8 (73) 2 (18) 1 (9)
Local recurrence-no (%)	2 (18)
Relapse free survival–months (median)	20
Distant metastases free survival – months (median)	23
Treatment status—no. (%) ongoing treatment with tebentafusp stopped treatment with tebentafusp dead progressed non evaluable tumor status	 6 (55) 5 (45) 3 (27) 5 (45) 3 (27)
Follow-up time after Tebe—months (median)	5.4
Lactate dehydrogenase—no. (%) <ULN >ULN > 2x ULN	 1 (9) 10 (91) 5 (45)
ECOG performance status—no. (%) 0 1 ≥2	 3 (27) 5 (45) 3 (27)
Site of metastases—no. (%) hepatic only hepatic and extrahepatic	 4 (36) 7 (64)
Preceding liver-directed therapy—no. (%)	2 (18)
Preceding systemic tumor therapy—no. (%)	2 (18)
Subseq/concom liver-directed therapy—no. (%)	1 (9)

Tab 1: Baseline characteristics of the patients. ULN = upper limit of normal; ECOG = Eastern Cooperative Oncology Group

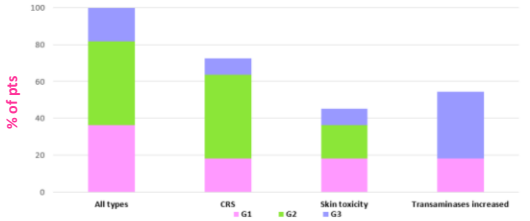

Fig.2: Frequency and severity of treatment-Related Adverse Events

Fig.3: Tumor response according to RECIST 1.1 in pts with at least one tumor assessment.

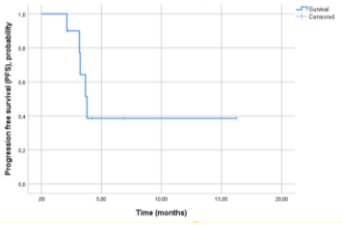

Fig.4: Progression-free survival (PFS)

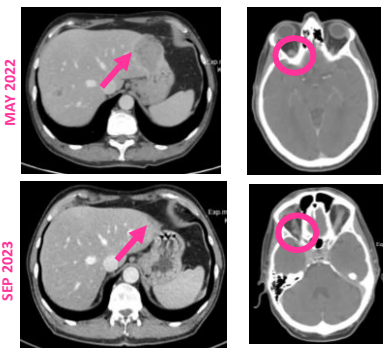

Fig.5 CT scan showing tumor burden reduction in the partial responding patient .

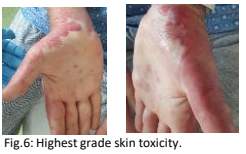

Fig.6: Highest grade skin toxicity.

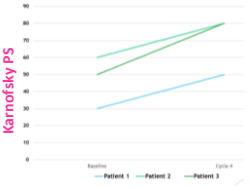

Fig.7: Performance Status (Karnofsky scale) changes after dose escalation phase in patients with poor PS at baseline.

REULTS AND CONCLUSIONS

In this rare and until now treatment orphan tumor we confirmed safety, response rate and PFS profile of Tebentafusp of published studies. A longer follow-up is necessary for OS evaluation. Although the limited number of patients, we often observed an early clinical benefit, that seemed to be independent from tumor burden and LDH levels.

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