Tebentafusp-tebn (KIMMTRAK)
National Drug Monograph
November 2024

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION

Description / MOA	Bispecific gp100 peptide-HLA-directed CD3 T-cell engager
Indication Under Review	HLA-A*02:01-postiive unresectable or metastatic uveal melanoma
Dosage Regimen	20mcg IV D1, 30mcg IV D8, 68mcg IV D15, then 68mcg IV weekly
Dosage Forms Under Review	Injection: 100mcg/0.5mL single-dose vial

EFFICACY CONSIDERATIO

Trial	IMCgp100-202 (Nathan, et.al.)[1] N=378 (n=252 Tebentafusp; n=126 chemo)
Design	OL, P3, MC, R for 1L treatment of metastatic HLA-A*02:01 Uveal melanoma Primary EP: OS
Population	Metastatic uveal melanoma, HLA-A*02:01 positive, no previous treatment, ECOG 0-1
Demographics	M 51%; PS 0 51%; LDH >ULN 36%; liver only 52%; extrahepatic only 4%; Liver and extrahepatic 44%
Intervention	Tebentafusp ramp-up then weekly
Comparator	Pembrolizumab or ipilimumab or dacarbazine Q21 days
Results	OS 1yr: 73%T vs 59% C; HR 0.51 (95%CI 0.37-0.71) mOS 21.7 vs 16 mos; PFS 6 mos: 31 vs 19%;
Notes	**NCCN Category 1A for HLA-A*02:01-positive tumors** **Other recommended regimens (cat 2A): Nivolumab+ipilimumab; for liver-only metastases: melphalan hepatic infusion, chemoembolization, resection plus radiation** **Consider in certain circumstances: dacarbazine, topotecan, paclitaxel, Abraxane, carboplatin/paclitaxel** **VA Oncology Clinical Pathway: Metastatic or recurrent HLA-A*02:01 positive uveal melanoma with metastases not limited to liver, following radiation for liver-only metastases, or not a candidate for resection and not a candidate for radiation** **Alternative options: if not HLA-A*02:01 positive, use nivolumab plus ipilimumab**

AFETY CONSIDERATIO

Boxed Warnings	Cytokine Release Syndrome (CRS)-monitor at least 16 hours after first 3 infusions
Contraindications	None
Other Warnings	CRS≥Gr2: 76%; Skin reactions: 91% (G3: 44%; G4: 21%); ↑LFT:65% (measure baseline AST/ALT/TBili); EF toxicity
Top 5 AEs	CRS, rash, pyrexia, pruritis, chills
Drug Interactions	None

VHA PLACE IN THERAPY

Potential Use in VHA

1. Initial 3 step-up doses in Cycle 1 require monitoring for at least 16 hours; if no Grade 2 or worse hypotension during or after third infusion, subsequent infusions require monitoring for at least 30 minutes
2. Facility must be equipped to monitor and manage Cytokine Release Syndrome (CRS) if needed
3. Metastatic or recurrent uveal melanoma that is HLA-*02:01 positive with metastases not limited to liver-only
4. Metastatic or recurrent uveal melanoma that is HLA-*02:01 positive and not a candidate for resection or radiation
5. Metastatic or recurrent uveal melanoma that is HLA-*02:01 positive with liver-only metastases following progression on liver-directed therapy

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References

[1] Nathan P, Hassel JC, Rutkowski P, et al. Overall survival benefit with tebentafusp in metastatic uveal melanoma. New Eng J Med 2021; 385: 1196-206.