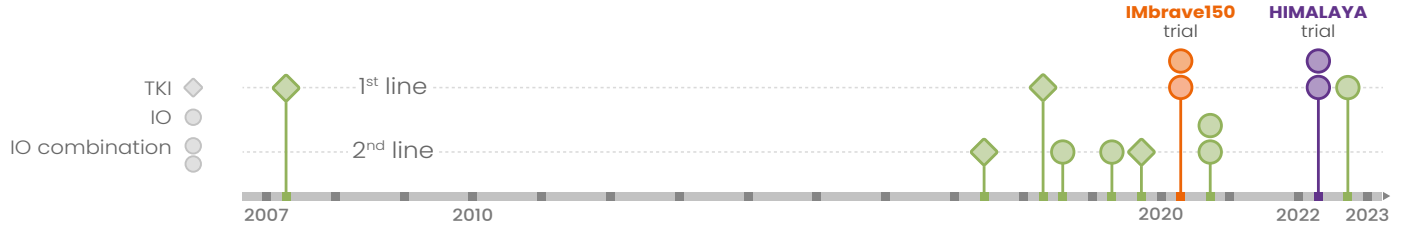
THE USE OF IMMUNOTHERAPY IN HCC

EFFICACY AND SAFETY

The systemic treatment landscape for patients with HCC has evolved rapidly over the last decade

These systemic treatment options can be TKIs, single agent immunotherapies (IO), or IO-based combinations.

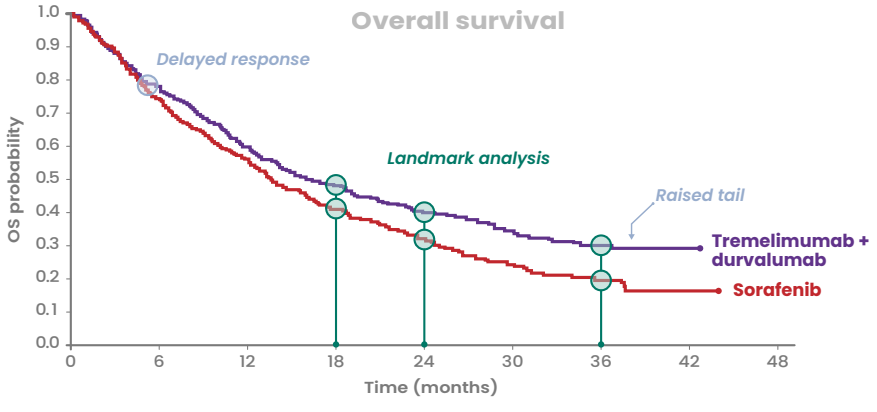


IO, and in particular IO combinations, are effective treatments for patients with advanced HCC

IO combination	**Atezolizumab (IO) + bevacizumab (anti-VEGF)** versus sorafenib[1] *Approved in* [2,3] 2020	**Tremelimumab (IO) + durvalumab (IO)** versus sorafenib[4] *Approved in* [5,6] 2022
Primary endpoint(s)	**OS and PFS**	**OS**
Key efficacy results	**Median OS (months)** Atezolizumab + bevacizumab: 19.2 Sorafenib: 13.4 HR (95% CI): 0.66 (0.52-0.85) **Median PFS (months)** Atezolizumab + bevacizumab: 6.9 Sorafenib: 4.3 HR (95% CI): 0.65 (0.53-0.81)	**Median OS (months)** Tremelimumab + durvalumab: 16.4 Sorafenib: 13.8 HR (96% CI): 0.78 (0.65-0.93) *Landmark analysis* **OS at 36 months (%)** Tremelimumab + durvalumab: 30.7 Sorafenib: 20.2

IO AND IO COMBINATIONS MAY RESULT IN INFLAMMATORY SIDE EFFECTS REFERRED TO AS irAES. MOST OF THESE ADVERSE EVENTS CAN BE TREATED WITH STEROIDS

Survival analysis for IO treatment shifts from median OS to landmark analysis



The **tail of the curve** is raised indicating an improved survival from a **durable response.**

This is **different from targeted therapies,** which typically show a quicker response, as shown by the early separation of the two curves, but **less durable**[7].

This **durable effect can be missed** when only looking at **median** progression free survival and **median** overall survival.

irAE, immune related adverse events; CI, confidence interval; HCC, hepatocellular carcinoma; HR, hazard ratio; IO, immunotherapy; OS, overall survival; PFS, progression free survival; TKI, tyrosine kinase inhibitor

1. Cheng, Ann-Lii, et al. Journal of hepatology. 2022;76(4):862-73; 2. FDA (2020). Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-atezolizumab-plus-bevacizumab-unresectable-hepatocellular-carcinoma (accessed March 2023); 3. EMA (2020). Available from: https://www.ema.europa.eu/en/documents/smop/chmp-post-authorisation-summary-positive-opinion-tecentriq-ii-39_en.pdf (accessed March 2023). 4. Abou-Alfa, Ghassan K, et al. NEJM Evidence. 2022;1.8; 5. FDA (2022). Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-tremelimumab-combination-durvalumab-unresectable-hepatocellular-carcinoma (accessed March 2023). 6. EMA (2022). Available from: https://www.ema.europa.eu/en/documents/smop-initial/chmp-summary-positive-opinion-imjudo_en.pdf (accessed March 2023); 7. Ribas, A., (2012). Clinical Cancer Research, 18(2), 336-341

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