Therapeutic Application of CXCR4 Antagonist DBPR807 for HCC Treatment

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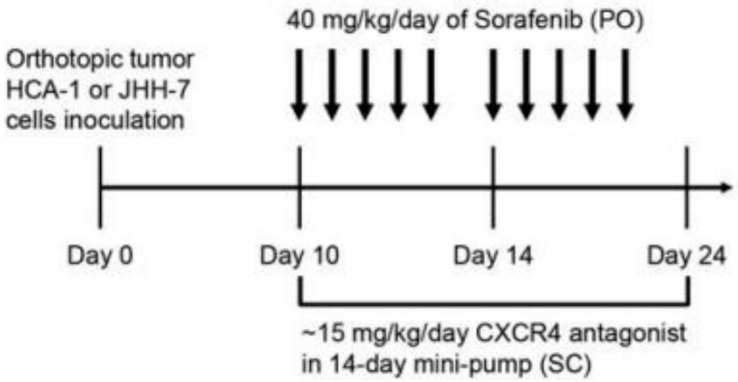
Disease Background and Market Analysis

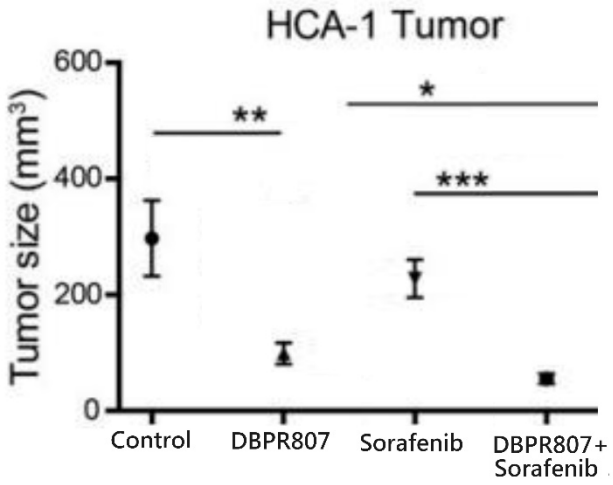
- Sorafenib is the first-line treatment for advanced Hepatocellular carcinoma (HCC), however sorafenib only offers a limited extension to survival time for patients with HCC as cancer metastasis and primary tumor relapse occur due to rapid sorafenib resistance.
- Sorafenib treatment reduces mean vessel density (MVD) and therefore elevates tumor hypoxia in HCC. This process significantly increases chemokine CXCL12 and chemokine receptor type 4 (CXCR4) expression and activates the CXCL12/CXCR4 pathway in HCC.
- To give the oncogenic potential of CXCL12/CXCR4 signaling, blockade of the CXCL12/CXCR4 axis might therefore synergize with current standard treatments. The combination of DBPR807 and sorafenib is a first-in-class of small molecule for HCC treatment. The market potential of DBPR807 will grow in tandem with the size of the sorafenib market (sorafenib sale: $729 million in 2020).

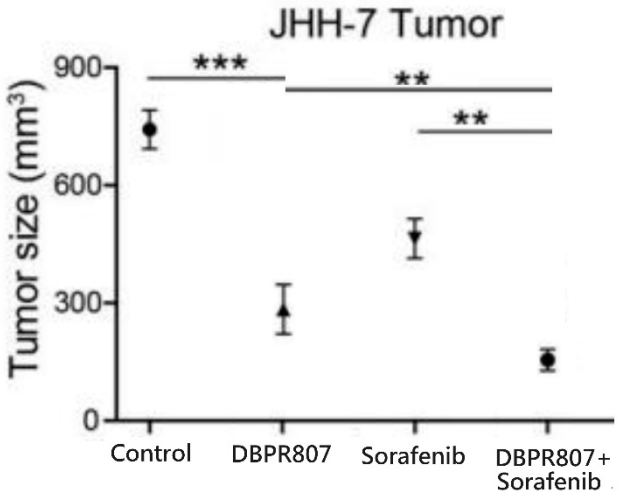
Approved Drug	Company	Target
Sorafenib	Bayer	VEGFR
Regorafenib	Bayer	VEGFR2
Nivolumab	BMS	Anti-PD-1
Lenvatinib	Eisai and Merck	VEGFR1-3
Pembrolizumab	Merck	Anti-PD-1
Cabozantinib	Exelixis	VEGFR2
Ramucirumab	Eli Lilly	VEGFR2
Nivolumab + Ipilimumab	BMS	Anti-PD-1 Anti-CTLA-4
Atezolizumab + bevacizumab	Genetech	Anti-PD-L1 Anti-VEGF

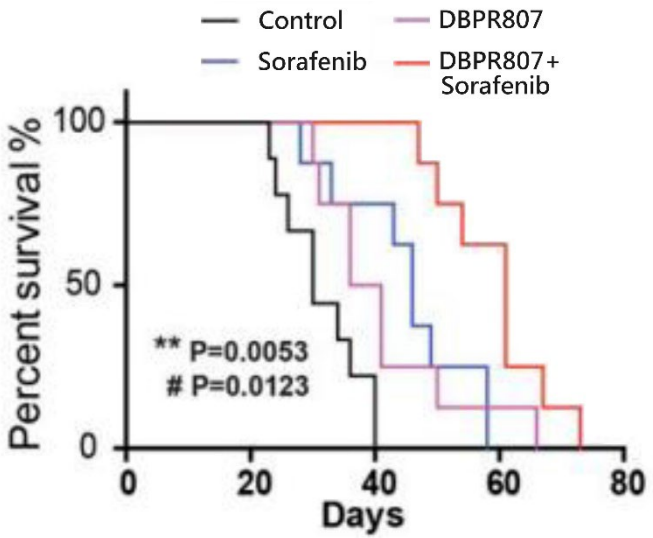
Product – Key Data or POC Data

DBPR807 Sensitizes HCC to Sorafenib Treatment in Orthotopic HCC Models









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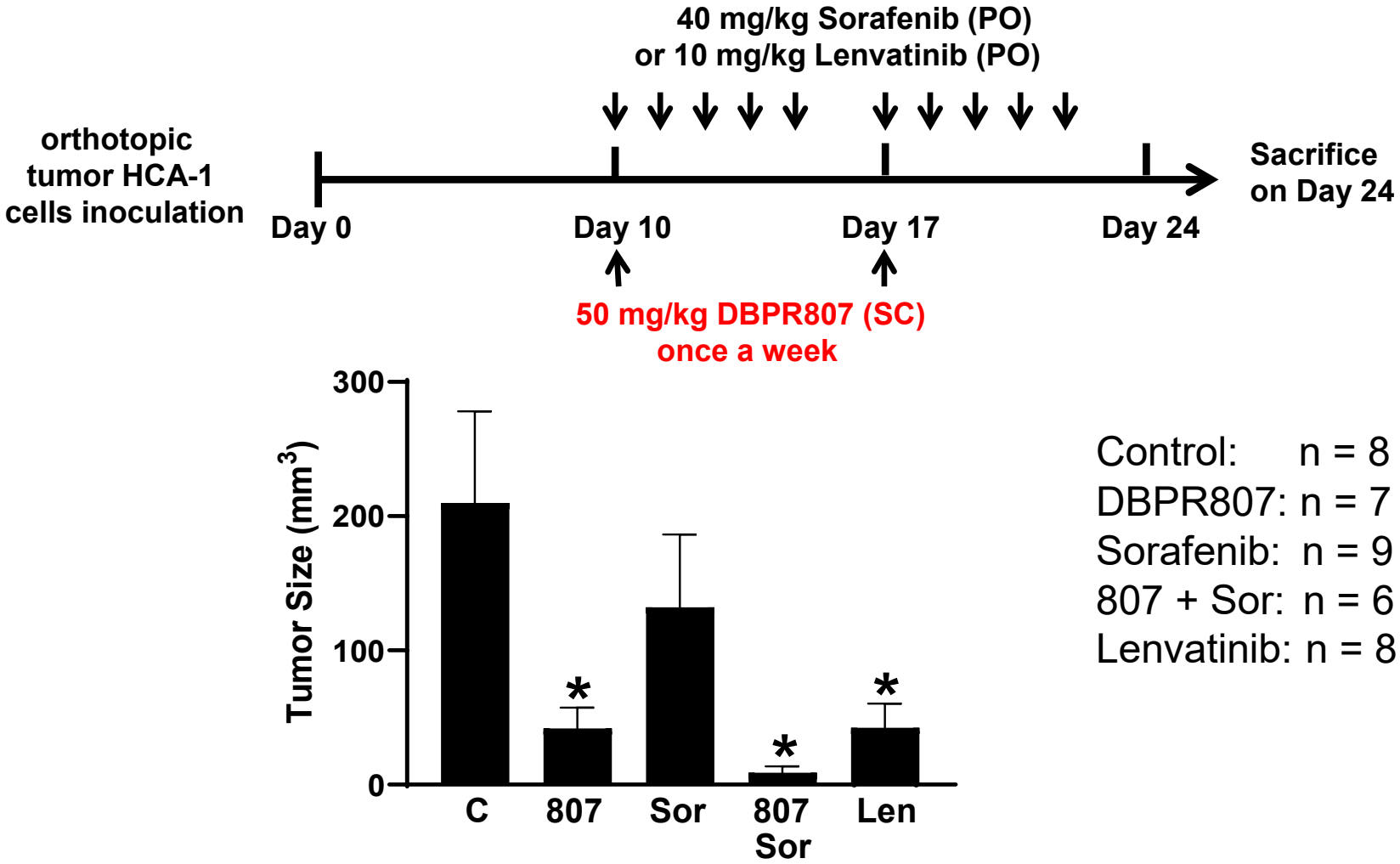
Product – Key Data or POC Data

Significant efficacy of DBPR807 (SC) in combination with Sorafenib



Control: n = 8
DBPR807: n = 7
Sorafenib: n = 9
807 + Sor: n = 6
Lenvatinib: n = 8

Product Summary

Key Features:

- DBPR807, a highly selective, safe, and potent CXCR4 antagonist, possesses better in vitro and in vivo efficacy than its marketed counterpart AMD3100 under various HCC settings with supreme benefits on combination therapy.
- DBPR807 can significantly synergize with not only antiangiogenic therapy (e.g. sorafenib) but also immunotherapy (e.g. anti–PD-1) to further extend overall survival in HCC models.
- Current results suggest the clinical treatment of DBPR807 for HCC might be administered at a dose of 50 mg/kg (SC) once weekly.

Intellectual Properties & Publication:

- TWI664174, US10882854, AU2018208366, JP6892716, CA3047146, NZ754272, RU2756055C2, KR102335082, IN379503.
- HCC disease indication: *Proc Natl Acad Sci USA*. **2021**; *118*(13): e2015433118.

Market Positioning:

- The combination of DBPR807 and sorafenib is a first-in-class and innovative therapeutic approach for boosting the efficacy of HCC treatment.