**Supplementary Materials**

# A systematic review of comparative economic analyses of systemic therapies for hepatocellular carcinoma

**Paolo De Simone[1,2], Daniela Peritore[3], Juri Ducci[4], Lucia Romano[5,6], Donato Longo[7], Antonio Giuliani[5,6], Daniela Campani[2,8], Fabio Vistoli[5,6]**

[1]Liver Transplant Program, University of Pisa Medical School Hospital, Pisa 56124, Italy.
[2]Department of Surgical, Medical, Biomolecular Pathology and Intensive Care, University of Pisa, Pisa 56126, Italy.
[3]Italian National Center for Transplantation, Rome 00162, Italy.
[4]Day-Surgery Unit, Pisa University Hospital, Pisa 56124, Italy.
[5]Division of General Surgery and Transplantation, San Salvatore Hospital, L'Aquila 67100, Italy.
[6]Department of Applied and Biotechnological Clinical Sciences, University of L'Aquila, L'Aquila 67100, Italy.
[7]Intensive Care Unit, Vito Fazzi Hospital, Lecce 73100, Italy.
[8]Pathology Department, Pisa University Hospital, Pisa 56124, Italy.

**Correspondence to:** Dr. Paolo De Simone, Liver Transplant Program, University of Pisa Medical School Hospital, Pisa 56124, Italy. E-mail: paolo.desimone@unipi.it

**Supplementary Table 1. Summary of systemic treatments for HCC approved in China (NMPA), the USA (FDA), and Europe (EMA)**

| Drug | China (NMPA) | USA (FDA) | Europe (EMA) | Study |
|---|---|---|---|---|
| **First-line drugs** | | | | |
| Sorafenib | 2008 | 2007 | 2007 | Phase III Asia-Pacific (AP) study, supported by data from the international SHARP trial |
| Oxaliplatin-containing regimens | 2013 | Off-label | Off-label | Phase III EACH study |
| Lenvatinib | 2018 | 2018 | 2018 | Phase III REFLECT study Chinese subgroup analysis |
| Donafenib | 2021 | None | None | Phase II/III ZGDH3 study |
| Atezolizumab + bevacizumab | 2020 | 2020 | 2020 | Phase III IMBrave -150 study |
| Sintilimab + bevacizumab biosimilar (IBI305) | 2021 | None | None | Phase II/III ORIENT-32 study |
| Camrelizumab + rivoceranib | 2023 | None | Orphan medicinal product designation for advanced HCC received in 2024 | Phase III CARES-310 study |
| Tislelizumab | 2023 | None | Orphan medicinal product | Phase III RATIONALE-301 |

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|---|---|---|---|---|
| | | | designation for advanced HCC received in 2022 | study |
| Pembrolizumab in combination with lenvatinib and TACE | 2025 | None | None | Phase III LEAP-012 trial |
| STRIDE | 2024 | 2022 | 2023 | Phase III HIMALAYA study |
| Nivolumab monotherapy | None | 2017 as second-line agent after sorafenib | None | Phase I/II Checkmate-040 study |
| Nivolumab + ipilimumab | Pending | 2020 as accelerated approval for previously treated HCC<br>In 2025 this approval was converted for first-line treatment | 2025 | Phase III Checkmate-9DW trial |
| **Second-line drugs** | | | | |
| Regorafenib after sorafenib | 2017 | 2017 | 2017 | Phase III RESORCE trial |
| Cabozantinib after sorafenib | 2019 | 2019 | 2018 | Phase III CELESTIAL trial |
| Apatinib (rivoceranib) after sorafenib | 2020 | None | None | Approval was based on increased off-label use |
| Pembrolizumab after sorafenib | None | 2018 | None | Phase III KEYNOTE-224 trial |

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|---|---|---|---|---|
| Ramucirumab after sorafenib for patients with AFP ≥ 400 ng/mL | 2022 | 2019 | 2020 | Phase III REACH-2 study |

AFP: Alfa-fetoprotein; EMA: European Medicinal Agency; FDA: Food and Drug Administration; HCC: hepatocellular carcinoma.