

Supplementary Table 2. Study design for hepatocellular carcinoma (HCC) treated with proton beam therapy (PBT)

Study	Nation	Institution	Study type	PBT indication	NOS
Uchinami et al., 2023 ²³	Japan	Hokkaido University Hospital	Retrospective	HCC ≤5 cm	5
Lizumi et al., 2023 ²⁴	Japan	University of Tsukuba	Retrospective	HCC with bile duct invasion, and not eligible or refusal for the standard Tx	5
Bush et al., 2023 ²⁵	USA	Loma Linda University Medical Center and the Jerry L. Pettis Memorial Veterans Hospital	Phase 3	Newly diagnosed HCC within the Milan or San Francisco criteria, but not eligible for S/R	8
Lin et al., 2021 ²⁶	Taiwan	Chang Gung Memorial Hospital, Linkou branch	Retrospective	HCC	5
Kim et al., 2021 ¹⁸	Korea	National Cancer Center	Phase 3	Recurrent or residual HCC with <3 cm and ≤2 lesions, but not eligible or refusal for surgery	8
Iwata et al., 2021 ²⁷	Japan	Nagoya Proton Therapy Center	Retrospective	HCC with age ≥80 years with T1-3N0M0 and ≤2 lesions	5
Iwata et al., 2021 ²⁸	Japan	Nagoya Proton Therapy Center	Phase 2	Operable or ablatable single HCC <12 cm (T1N0M0*), but refusal for LRT	5
Yoo et al., 2020 ²⁹	Korea	Samsung Medical Center	Retrospective	Not eligible for S/R	4
Tamura et al., 2020 ³⁰	Japan	Shizuoka Cancer Center Hospital	Retrospective	Single HCC ≤10 cm without VI	7
Hojo et al., 2020 ³¹	Japan	National Cancer Center Hospital East, Chiba	Retrospective	Not eligible or refusal for S/R	5
Sanford et al., 2019 ³²	USA	Massachusetts General Hospital	Retrospective	Inoperable HCC	7
Kim et al., 2019 ³³	Korea	National Cancer Center	Retrospective	Not eligible or refusal for LRT	5
Chadha et al., 2019 ³⁴	USA	The University of Texas MD Anderson Cancer Center	Retrospective	Inoperable HCC that is >1 cm away from GI tract	5
Mizuhata et al., 2018 ³⁵	Japan	Fukui Prefectural Hospital	Retrospective	Not eligible or refusal for S/R and adjacent to the GI tract ≤2 cm	5
Kimura et al., 2017 ³⁶	Japan	Southern Tohoku Proton Beam Therapy Center	Retrospective	Single HCC ≥5 cm, but not eligible or refusal for surgery	5
Kim et al., 2015 ³⁷	Korea	National Cancer Center	Phase 1	Inoperable HCC ≤10 cm	5
Lee et al., 2014 ³⁸	Korea	National Cancer Center	Retrospective	HCC with PVTT	4
Mizumoto et al., 2011 ³⁹	Japan	University of Tsukuba	Retrospective	HCC	5
Komatsu et al., 2011 ⁴⁰	Japan	Hyogo Ion Beam Medical Center	Retrospective	HCC ≤15 cm	5
Kawashima et al., 2011 ⁴¹	Japan	National Cancer Center Hospital East, Chiba	Retrospective	HCC ≤10 cm	5
Chiba et al., 2005 ⁴²	Japan	University of Tsukuba	Retrospective	Not eligible or refusal for LRT with ≤3 lesions	5
Bush et al., 2004 ⁴³	USA	Loma Linda University Medical Center	Phase 2	HCC with T1-4 [†]	5

NOS, the Newcastle-Ottawa scale; Tx, treatment; S/R, surgery or radiofrequency ablation; LRT, locoregional treatment including surgery, radiofrequency ablation, or transarterial chemo-embolization; VI, vascular invasion; GI, gastrointestinal; PVTT, portal vein tumor thrombosis.

* Staged according to the seventh edition of International Union Against Cancer staging system; [†] Staged according to the 1998 version of the American Joint Committee on Cancer staging system.