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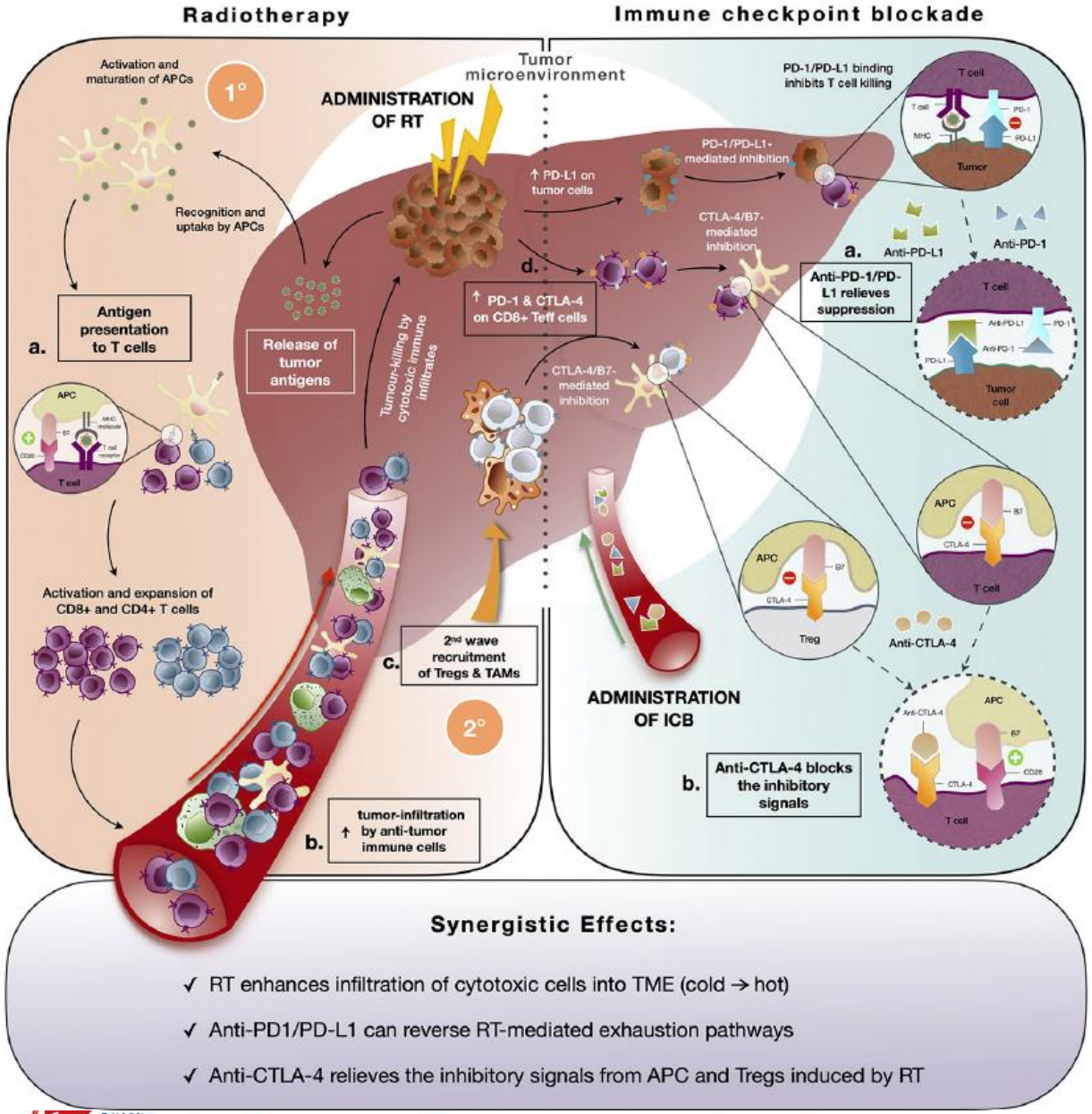
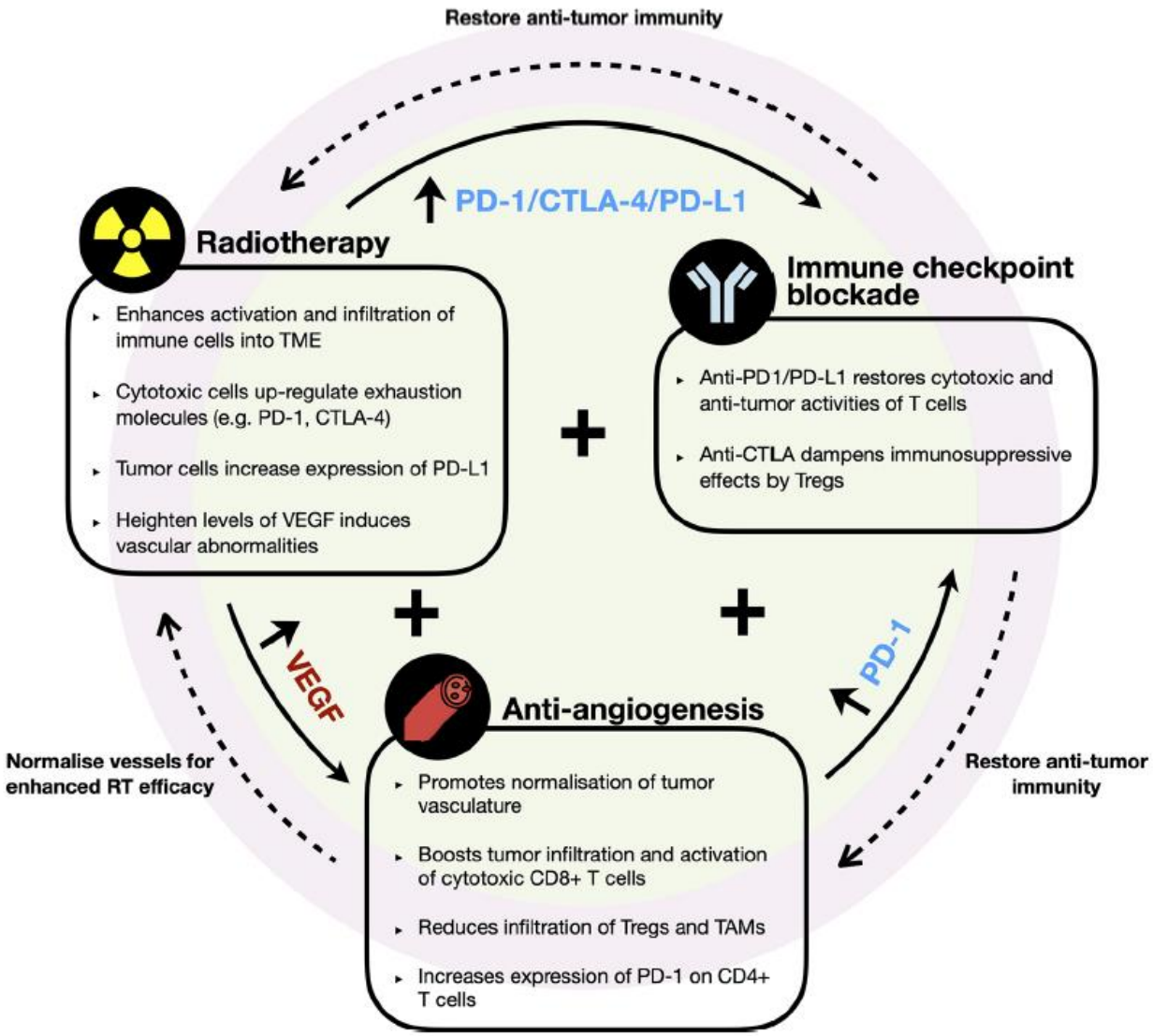
Feasibility of Additional Radiotherapy for Advanced Hepatocellular Carcinoma Patients treated with Atezolizumab plus Bevacizumab

Tae Hyun Kim[1,2], Bo Hyun Kim[1], Yu Ri Cho[1], Eun Sang Oh[2], Joo-Hyun Chung[2], Young-Hwan Koh[1], Joong-Won Park[1]

[1]Center for Liver and Pancreatobiliary Cancer, National Cancer Center, Goyang, 10408, Korea
[2]Center for Proton Therapy, National Cancer Center, Goyang, 10408, Korea

RT (Radiotherapy) + Immunotherapy





Lee YH et al. Front Immunol 2020;11:568759

Feasibility of Additional RT in Advanced HCC Treated with Ate/Beva

- Between March 2021 and October 2021, NCC, Korea

Pt.	Age	Sex	ECOG PS	CP score / ALBI score	AJCC/BCLC Stage	Initial Tx	Targeted Lesion(s) to RT	Dz. Status other than Targeted Lesion(s)	Size of Targeted Lesion(s) (cm)	Prev. Tx to Targeted Lesion(s)
1	77	M	0	5 / 2	T1N0M0/A rT3aN0M1/C	TACE→ SR→TACE	P seeding	No	6.5	TACE → Ate/Beva
2	64	M	0	7 / 3	T3bN0M0/C	-	BM TT	IHD	4.6	TACE → Ate/Beva
3	57	M	0	7 / 2	T3bN0M0/C	-	BM, IVC TT	IHD	7.0	Ate/Beva
4	50	M	0	8 / 3	T3aN0M0/C rT3bN0M0/C	TACE→Ate/Beva	BM TT	IHM	4.6	Ate/Beva
5	39	M	0	6 / 2	T1N0M0/A rT0N0M1/C	SR	P seeding	EHD	13.0	Ate/Beva
6	65	M	1	7 / 3	T3bN0M1/C	-	Bone	IHD/EHD	6.2	Ate/Beva
7	49	M	0	5 / 2	T3aN1M1/C	-	Adr GI, PAN	IHD/EHD	3.0	Ate/Beva

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- Treatment details and outcomes of patients receiving additional radiotherapy (RT)

Pt.	Type of RT	TD (Gy) / fractions	Subseq. Tx after RT	TLR / OR	Site(s) of PD	Subseq. Tx after PD	TI to LP (mo)	TI to PFS (mo)	TI to OS (mo)
1	PBT	66 / 10	Ate/Beva	CR / CR	IHD/EHD	RT→Ate/Beva→TACE→Lenva	-	4.8	DWD 14.9
2	PBT	35 / 10	Ate/Beva	PR / SD	IHD	Ate/Beva→Ate/Lenva	-	4.0	DWD 13.5
3	IMRT	35 / 10	Ate/Beva	PR / SD	-	-	-	-	DWD 13.7
4	IMRT	35 / 10	Ate/Beva	SD / SD	IHD	-	-	2.8	DWD 4.2
5	IMRT	33 / 10	Ate/Beva	SD / SD	EHD	RT→Ate/Beva→SR→Lenva	5.9	3.9	DWD 14.8
6	IMRT	66 / 10	Ate/Beva	PR / PD	IHD/EHD	-	-	2.6	DWD 16.1
7	IMRT	33 / 10	Ate/Beva	PR / PR	EHD	Nivo + GP	7.2	7.2	AWD 14.2

Abbreviations: TD, total radiation dose; Gy, gray; Subseg., subsequent; TLR, targeted lesion(s) response; OR, overall response; PD, progressive disease; TI, time interval; LP, local progression; PFS, progression free survival; OS, overall survival; mo, months; PBT, proton beam therapy; IMRT, intensity modulated radiotherapy; TACE, trasarterial chemoemboization; Lenva, lenvatinib; Nivo, nivolumab; GP, gemcitabine and cisplatin; CR, complete response; PR, partial response; SD, stable disease; DWD, death with disease; AWD, alive with disease; and the other terms are the same as in Table 1.

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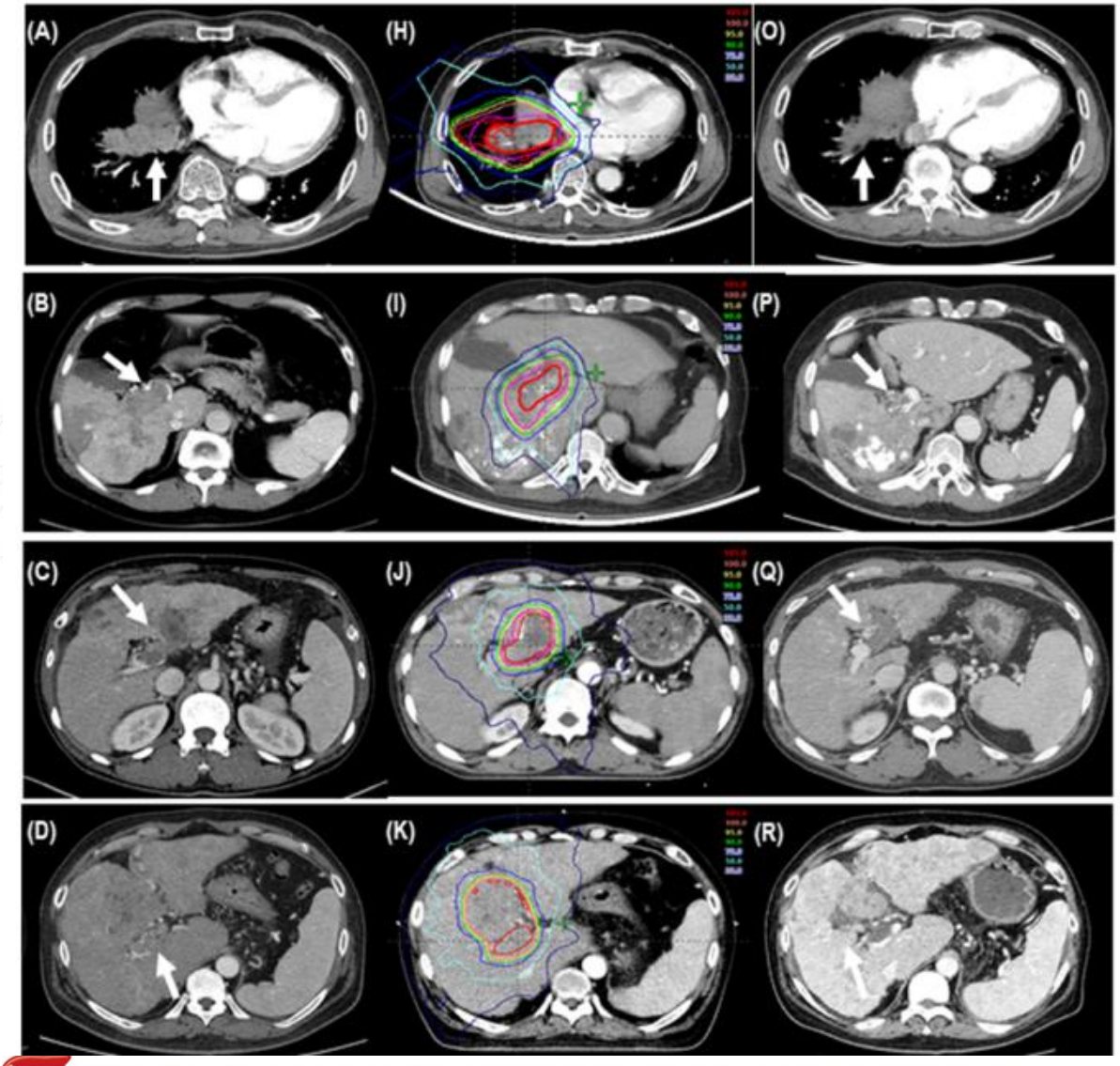
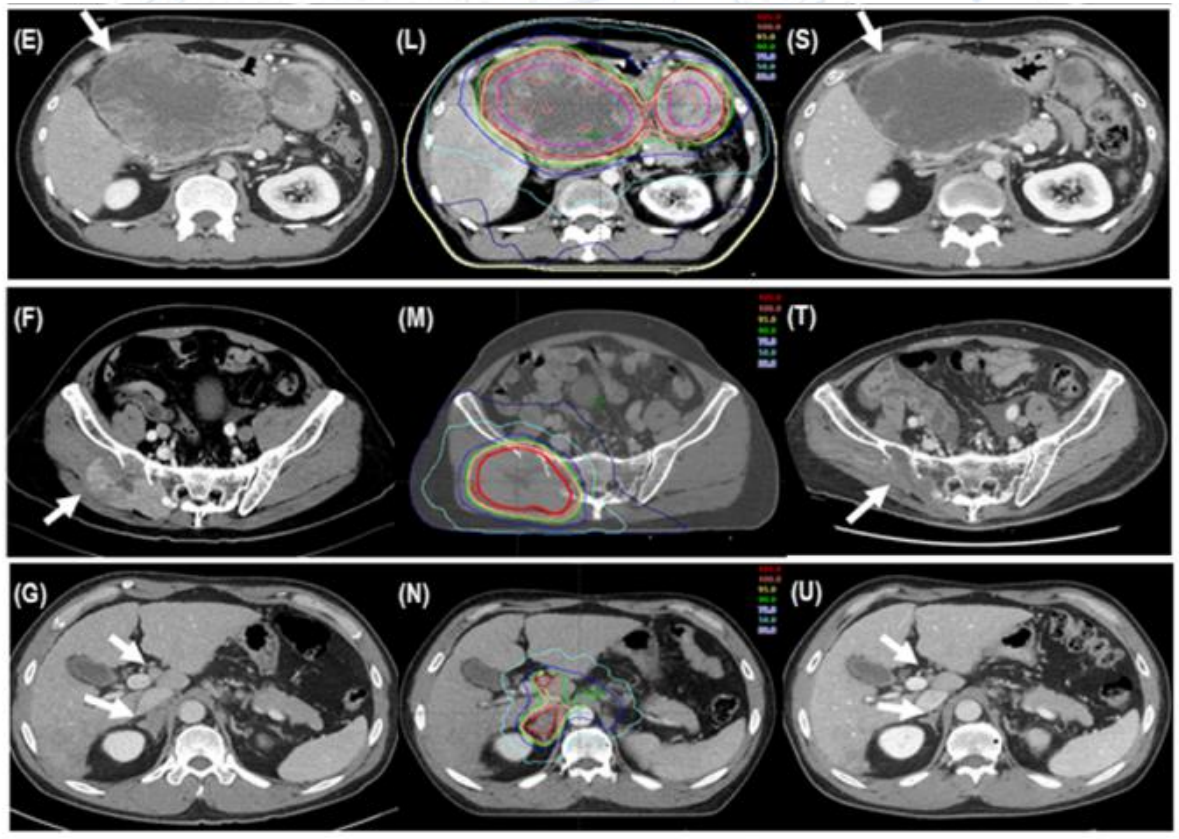
- Tumor responses of Targeted lesion(s) to RT (Radiotherapy)

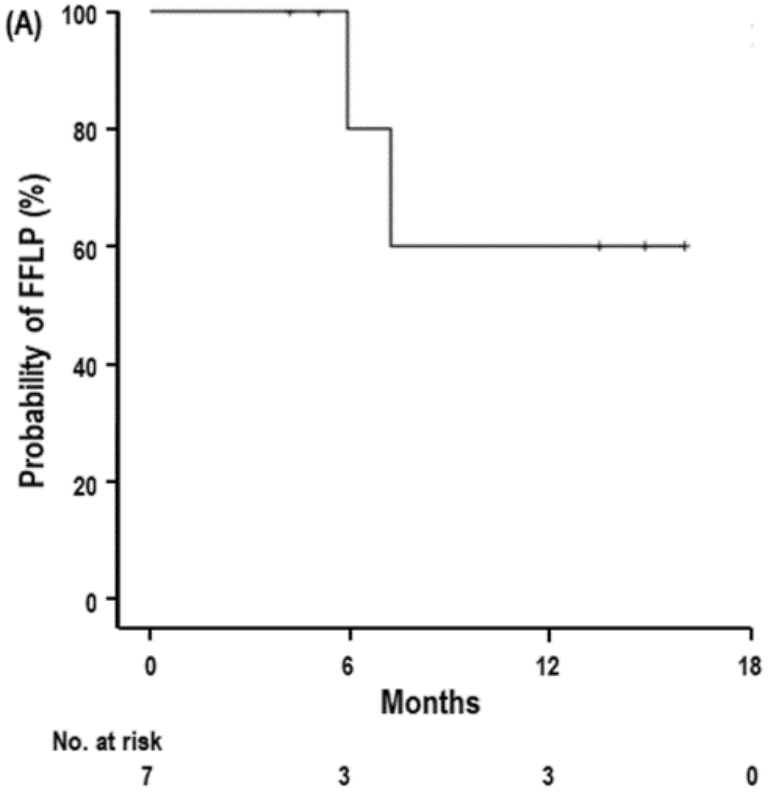


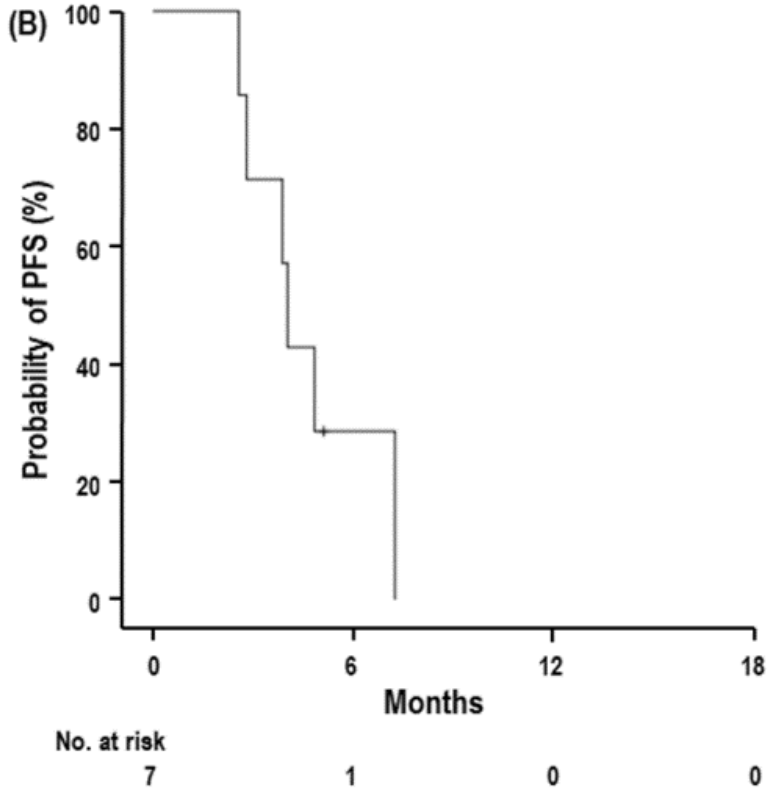


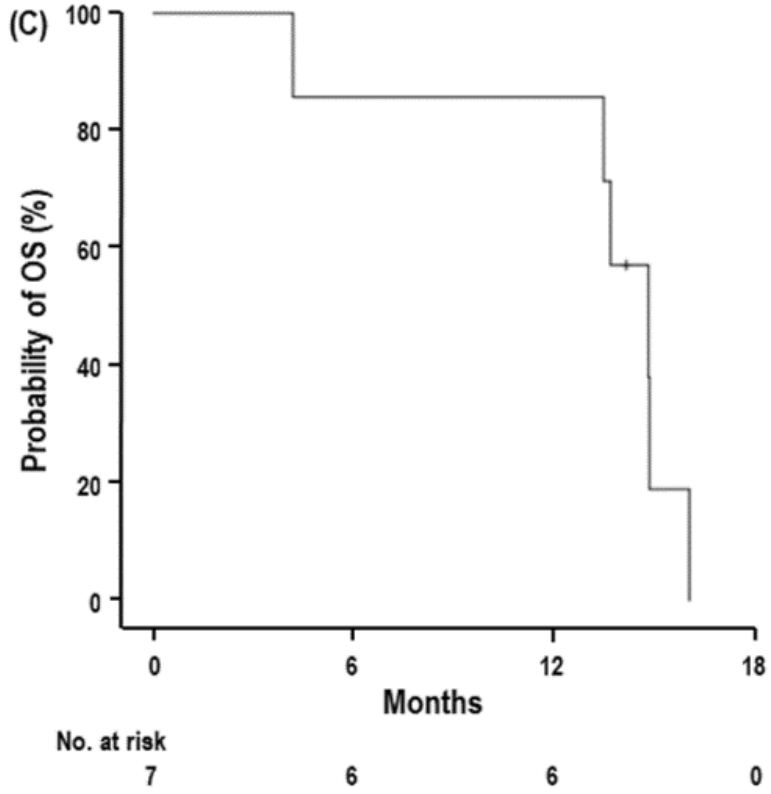
A, B, C, D, E, F, and G: Pre-treatment computed tomography (CT) scans showing the targeted lesion (s) of radiotherapy (RT) (arrow) in each patient (No. 1 – 7, respectively). H, I, J, G, K, L, M, and N: RT (33 – 66 Gy in 10 fractions) in each patient (No. 1 – 7, respectively). O, P, Q, R, S, T, and U: CT scans at 2 – 3 months after RT showing response of targeted lesion (s) (arrow) in each patient (No.1 – 7, respectively).

Feasibility of Additional RT in Advanced HCC Treated with Ate/Beva

- FFLP (Free From Local Progression), PFS (Progression-Free Survival), and OS (Overall Survival) after RT







Median: -
1-yr FFLP: 60 %(95% CI, 43.8 – 76.2)

Median: 4.0 mo (3.6 – 4.5)
1-yr PFS: 0 %(95% CI, -)

Median: 14.8 mo (95% CI, 12.5 – 17.2)
1-yr OS: 85.7%(95% CI, 75.9 – 95.5)

Kim TH et al. JLC 2023 (In press)

Feasibility of Additional RT in Advanced HCC Treated with Ate/Beva

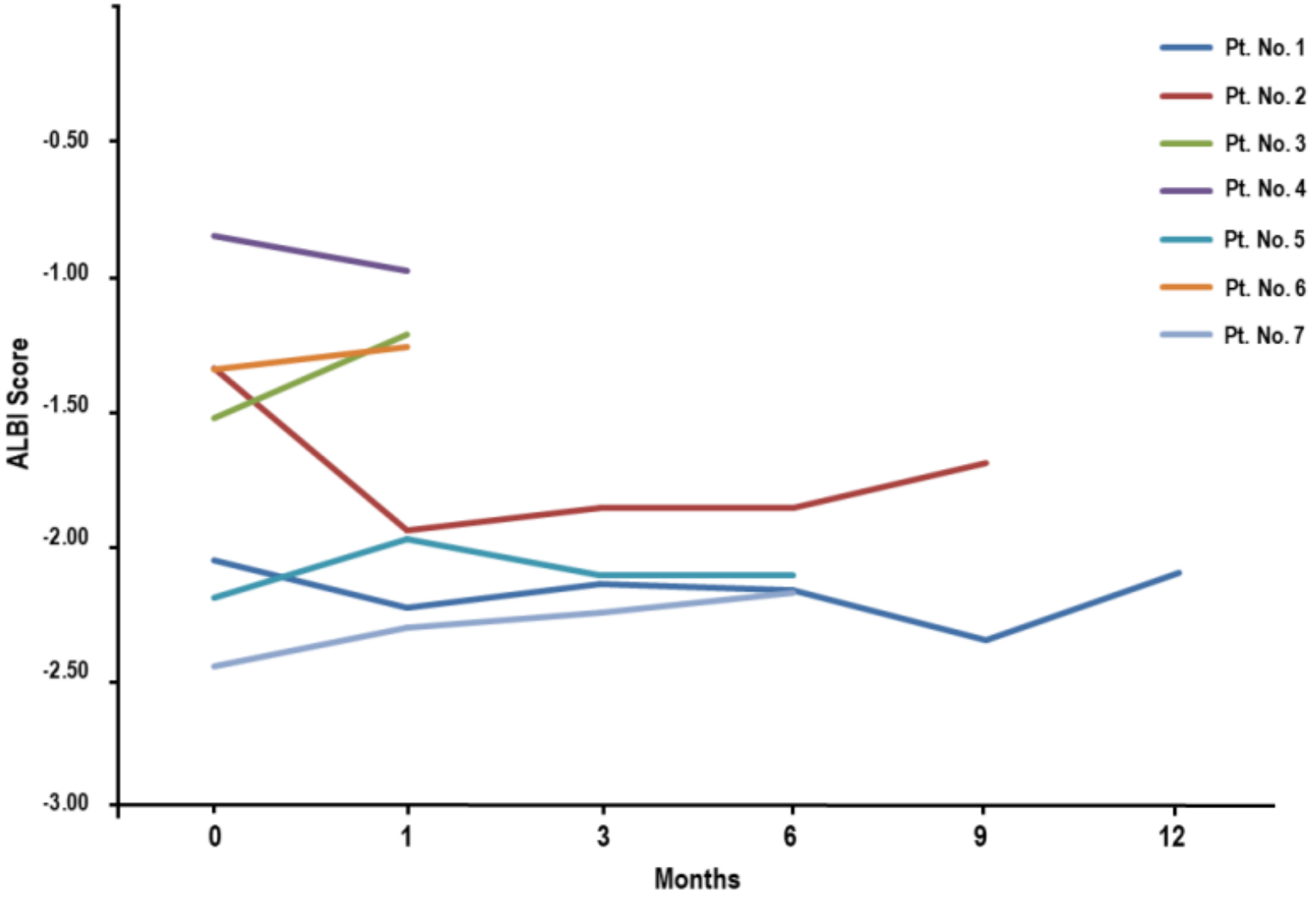
- **Adverse Events during and after RT in HCC treated with Ate/Beva**

	All patients (n = 7)			
CTCAE grade	Grade 1, n(%)	Grade 2, n(%)	Grade 3, n(%)	Grade 4, n(%)
Hematologic AEs	3 (42.9)	4 (57.1)	0 (0.0)	0 (0.0)
WBC increase	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)
WBC decrease	3 (42.9)	3 (42.9)	0 (0.0)	0 (0.0)
PLT decrease	1(14.3)	2 (28.6)	0 (0.0)	0 (0.0)
ALT/AST increase	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)
Albumin decrease	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)
Bilirubin increase	1 (14.3	0 (0.0)	0 (0.0)	0 (0.0)
Non-hematologic AEs	1 (14.3)	1 (14.3)	1 (14.3)	0 (0.0)
Fever	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)
Pain	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dermatitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Radiation pneumonitis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Bleeding	0 (0.0)	1 (14.3) *	1 (14.3)†	0 (0.0)

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; (Version 5.0); n., number of patients; WBC, white blood cell; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase

Feasibility of Additional RT in Advanced HCC Treated with Ate/Beva

- Changes in ALBI score after treatment with RT and Ate/Beva



Abbreviations: ALBI score, albumin-bilirubin score; Pt., patient; and No., number.

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- **Limitations:**

➢ **Thorough analysis for prognostic and confounding factors, including Targeted lesions to RT, Sequence between RT and Ate/Beva, Disease status, Liver function status, etc., due to retrospective study with small number of study populations.**

➢ **Probability of underestimation of AEs in retrospective studies: recall bias, incompleteness of medical records, etc.**

- **Conclusion**

➢ **The addition of RT may be a feasible and potentially effective treatment option for patients with advanced HCC treated with atezolizumab plus bevacizumab, and the addition of RT was well tolerated.**

➢ **Further studies are required to validate these findings and assess the safety and efficacy of this treatment approach.**