INTERIM RESULTS FROM THE PROSPECTIVE NATIONAL INTERSECTORAL COHORT STUDY JADE

REAL-WORLD TREATMENT PATTERNS AND OUTCOMES IN AND BEYOND FIRST-LINE IMMUNE CHECKPOINT INHIBITION IN PATIENTS WITH HCC

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INTRODUCTION

With the approval of immune checkpoint inhibitors (ICI) in 2020, 2023, and most recently in 2025, the survival rates of patients with advanced hepatocellular carcinoma (HCC) improved. While studies had shown a benefit for second-line tyrosine kinase inhibitors (TKI) after first-line TKI, it is unclear which second-line regimen should be administered following ICI (combination) treatment and phase 3 evidence is missing.

PATIENTS AND METHODS

Here, we present interim results from the prospective, multicenter, intersectoral, longitudinal cohort study JADE (NCT04510740) collecting data on patients with HCC from 105 sites in Germany since August 2020. Here, we present patient and tumor characteristics, systemic treatments and outcome data for patients with intermediate- or advanced-stage HCC (BCLC B/C/D or UICC III-IV) treated with ICI in first line.

RESULTS

Until April 30, 2025, 618 patients with HCC were enrolled and evaluable for analysis. In JADE, patients can be enrolled at start of any type of treatment (surgery, locoregional treatment or systemic treatment). Here, we present data of a subset of 339 patients with newly diagnosed intermediate – or advanced stage HCC treated initially with ICI mono- or combination therapy in first line **(Figure 1)**.

Of all evaluable patients with ICI treatment, 265 patients (78 %) received atezolizumab and bevacizumab (ATZ+BEV), 58 patients (17 %) received durvalumab and tremelimumab (DUR+TRE), 7 patients (2%) received ATZ monotherapy and 6 patients (2 %) received DUR monotherapy. **(Figure 2)**.

Patient characteristics are outlined in **Table 1:** Patients were mainly male (274 patients, 81 %), median age at treatment start was 72 years, 85 patients (25 %) had an ECOG of 0, 180 patients (53 %) had an ECOG of 1 and 50 patients (15 %) had an ECOG PS of ≥ 2. Almost all patients (97 %) had at least one comorbidity, 235 patients (69 %) had a Charlson comorbidity index of ≥ 1. BCLC stage at inclusion was B/C/D for 22 %/71 %/7 % while Child-Pugh score was A/B/C for 55 %/19 %/4 % of the patients.

At database cut for this interim analysis, 77 of 339 patients (23 %) received a second line ('Treated'), in 80 patients (24 %) the first line was still ongoing, or a therapy break was documented ('Potential'), 151 patients (45 %) deceased after the first line ('Died') and 31 patients (9 %) were lost to follow-up ('LTFU') **(Figure 3)**.

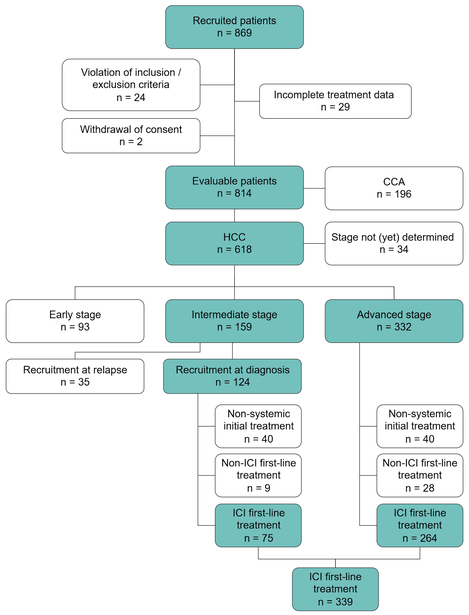
In case patients received a second line, the most frequent second-line regimen was sorafenib (n = 53, 69 %) followed by cabozantinib and lenvatinib in 9 patients (12 %) each **(Figure 4)**. A third-line regimen was administered to 23 patients (7 % of all 339 patients who had started first line), thereof 16 patients (70 %) received cabozantinib **(Figure 5)**. Overall, the most frequently used treatment sequence was treatment with atezolizumab in combination with bevacizumab (ATZ+BEV) in first line followed by target inhibitor treatment in second line (sorafenib (SOR)) as well as in third line (cabozantinib (CAB)) **(Figure 6)**.

The analyses on outcome data are restricted to patients who started their line of treatment at least 12 months before database cut (treatment start before April 30, 2024) comprising 275 of the 336 patients. Median progression-free survival (PFS) of first-line ICI therapy (ATZ+BEV, ATZ, DUR+TRE or DUR) was 7.4 months (95 % CI 5.1, 9.0) in patients with BCLC stage B and 4.1 months (95 % CI 3.3; 5.0) in patients with BCLC stage C **(Figure 7)**, median PFS in all evaluable patients was 4.7 months (95 % CI 3.8, 5.5) (data not shown). Median PFS of second-line therapy was 3.4 months (95 % CI 2.9, 5.3) and 3.5 months [95 % CI 1.5, 4.3] in third line (data not shown). Median overall survival was 8.4 months (95 % CI 6.5, 17.2) in patients with BCLC stage B and 9.0 months (95 % CI 6.7, 11.6) in patients with BCLC stage C **(Figure 8)** and 8.8 months (95 % CI 7.1, 11.2) in all evaluable patients (data not shown).

FAZIT

In real world, ICIs are the new first-line standard of care for patients with HCC. Although there is no evidence from phase 3 trials regarding second-line treatment after ICI-based first-line therapy, TKIs are the second-line standard of care following ICIs.

Figure 1: HCC patients with initial immune checkpoint inhibitor systemic treatment (n = 339)



Patients with newly diagnosed intermediate stage (BCLC B / UICC III) or advanced stage (BCLC C/D / UICC IV) recruited between August 2020 and April 2025 were included. Note: The category "Non-systemic initial treatment" includes patients who received surgery or locoregional therapy (e.g. ablation, TACE or SIRT) as initial treatment after inclusion.

Table 1: Patient characteristics at start of treatment

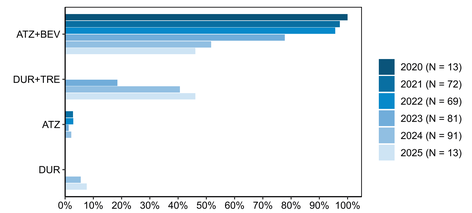
	Total
Patients (N)	**339**
Sex	
Female	65 (19.2%)
Male	274 (80.8%)
Age at start of treatment [years]	
Median (25%/75% quantiles)	72 (66 - 78)
ECOG performance status at start of treatment	
0	85 (25.1%)
1	180 (53.1%)
≥2	50 (14.7%)
Unknown to site	15 (4.4%)
Missing	9 (2.7%)
Any comorbidity	
Yes	329 (97.1%)
No	10 (2.9%)
Charlson Comorbidity Index (CCI) [0-24]	
0	104 (30.7%)
1	31 (9.1%)
≥2	204 (60.2%)

Table 1: Patient characteristics at start of treatment

	Total
Patients (N)	**339**
Barcelona Clinic Liver Cancer (BCLC)	
0-A	0 (0.0%)
B	73 (21.5%)
C	240 (70.8%)
D	22 (6.5%)
Not determined/unknown	4 (1.2%)
Child-Pugh Score	
A	186 (54.9%)
B	64 (18.9%)
C	14 (4.1%)
Missing	75 (22.1%)

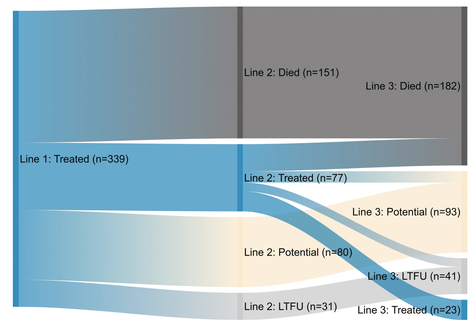
Any comorbidity: comorbidities according to CCI and other comorbidities combined. CCI (at inclusion): Comorbidities according to Charlson (Charlson et al. 1987), current weighting according to Quan (Quan et al. 2011). Range 0 – 24.

Figure 2: Relative frequencies of most applied first line ICI treatment regimens by year



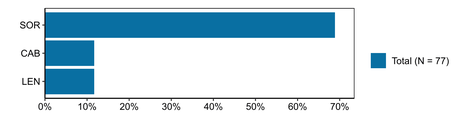
Regimens are presented as documented by the sites. Regimens including drugs documented by study sites as "other" or experimental drugs are not shown.
The year 2020 comprises five and the year 2025 comprises four months.
Date of approval ATZ+BEV: October 27, 2020, date of approval DUR+TRE: November 15, 2023.

Figure 3: Patient follow-up status



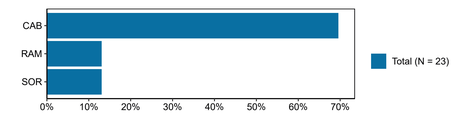
Treated – Treatment in the respective line received | Potential – Patients who might still receive a subsequent line of treatment (e.g. prior treatment still ongoing) | LTFU – Lost to follow-up after previous line or prior to respective line of treatment | Died – Patient died prior to beginning of indicated line.

Figure 4: Relative frequencies of most applied second line treatment regimens



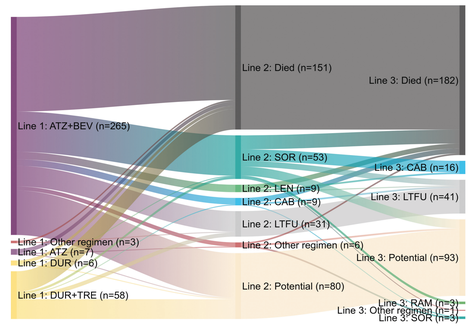
Regimens are presented as documented by the sites. Regimens including drugs documented by study sites as "other" or experimental drugs are not shown.

Figure 5: Relative frequencies of most applied third line treatment regimens



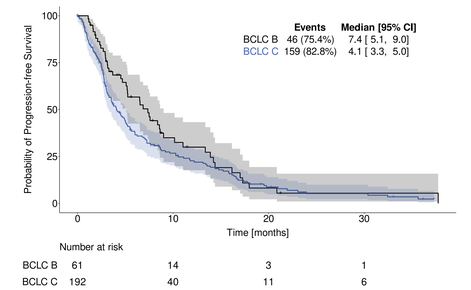
Regimens are presented as documented by the sites. Regimens including drugs documented by study sites as "other" or experimental drugs are not shown.

Figure 6: Sequential treatment regimens and patient follow up status first to third line.



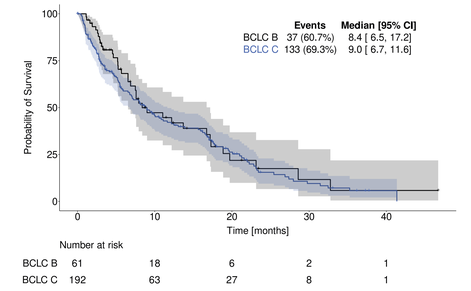
The category "Other treatment" comprises treatment regimens with less than three treatments as well as regimens documented as other e.g. study medication. Potential – Patients who might still receive a subsequent line of treatment (e.g. prior treatment still ongoing). LTFU – Lost to follow-up after previous line or prior to respective line of treatment. Died – Patient died prior to beginning of indicated line.

Figure 7: Progression-free survival – ICI first-line - outcome sample – BCLC B and BCLC C patients.



Outcome sample: Patients who started their line of treatment at least 12 months before database cut (treatment start before April 30, 2024) were included for analysis. PFS determines the time from the start of the systemic treatment to the event (progression of the disease or death), taking into account patients who are alive and progression-free at database cut (censored cases).

Figure 8: Overall survival – ICI first-line - outcome sample – BCLC B and BCLC C patients.



Outcome sample: Patients who started their line of treatment at least 12 months before database cut (treatment start before April 30, 2024) were included for analysis. OS determines the time from the start of the systemic treatment to the event (death), taking into account patients who are alive at database cut (censored cases).

Abbreviations:

BCLC: Barcelona Clinic Liver Cancer | CI: confidence interval | HCC: hepatocellular carcinoma | ICI: immune checkpoint inhibitor | OS: overall survival | PFS: progression-free survival | TKI: tyrosine kinase inhibitor | UICC: Union Internationale contre le cancer | ATZ: atezolizumab | BEV: bevacizumab | CAB: cabozantinib | DUR: durvalumab | LEN: lenvatinib | SOR: sorafenib | TRE: tremelimumab

References:

Charlson, M.E., Pompei, P., Ales, K.L., and MacKenzie, C.R., 1987. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. Journal of Chronic Diseases, 40 5, 373-383. doi:10.1016/0021-9681(87)90171-8.

Quan, H. et al., 2011. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. American journal of epidemiology, 173 6, 676–682. doi:10.1093/aje/kwq433.

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Conflicts of interest, personal:

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