

IMPACT OF RISK FACTORS ON OVERALL SURVIVAL IN PATIENTS WITH UNRESECTABLE HEPATOCELLULAR CARCINOMA TREATED WITH FIRST-LINE TISELIZUMAB

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Conclusions

Risk factors may impact overall survival (OS) in first-line (1L) treatment for patients with unresectable hepatocellular carcinoma (HCC). This exploratory analysis from RATIONALE-301 suggests that albumin-bilirubin (ALBI) grade could have prognostic value for OS, irrespective of treatment.

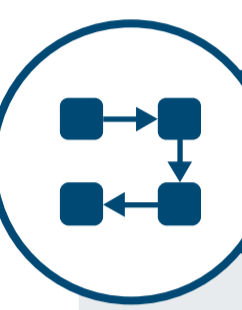
For patients with a more favorable balance between systemic inflammation and immunity, tislelizumab demonstrated numerically improved median OS compared with sorafenib for platelet-lymphocyte ratio (PLR) ≤ 141 , and neutrophil-lymphocyte ratio (NLR) ≤ 3 . For patients with PLR > 141 or NLR > 3 median OS was longer on sorafenib.



Background

- HCC is one of the leading causes of cancer-related death worldwide.¹ Most patients present with advanced disease and therefore have a poor prognosis.² Certain HCC biomarkers may be prognostic factors, with a potential clinical role in the 1L treatment of unresectable HCC¹
- Tislelizumab is a humanized monoclonal antibody with high affinity and binding specificity for programmed cell death protein 1, which was specifically engineered to minimize Fcγ receptor binding on macrophages²⁻⁴

- In the phase 3 RATIONALE-301 trial (NCT03412773), tislelizumab demonstrated noninferior OS versus sorafenib as 1L monotherapy for unresectable HCC (median OS 15.9 vs 14.1 months, respectively; hazard ratio 0.85), with a favorable safety profile⁵
- This exploratory analysis examined the effects of ALBI grade, platelet count, PLR, and NLR as predictors of OS in RATIONALE-301



Methods

- The study design has been previously described^{2,5}
- Systemic therapy-naïve adults with histologically confirmed, unresectable HCC were randomized (1:1) to receive tislelizumab 200 mg intravenously every 3 weeks or sorafenib 400 mg orally twice a day until disease progression, intolerable toxicity, or withdrawal of consent
- The primary endpoint was OS; key secondary endpoints included objective response rate, progression-free survival, and duration of response by blinded independent review committee, per RECIST v1.1; safety was also investigated
- This exploratory analysis examined OS in subgroups of patients defined by ALBI grade (≥ 2 vs 1), platelet count ($> 150K$ vs $\leq 150K$), PLR (> 141 vs ≤ 141), and NLR (> 3 vs ≤ 3) as predictors of OS



Results

Baseline Characteristics

- At data cutoff (July 11, 2022), minimum study follow-up was 33 months
- Demographics and baseline characteristics for biomarkers were generally balanced across arms (Table 1)

Prognostic Biomarkers Analysis

- Tislelizumab demonstrated numerically longer (≥ 3 months) median OS versus sorafenib in the biomarker subgroup categories ALBI grade 1 (Figure 1), NLR ≤ 3 (Figure 2), and PLR ≤ 141 (Figure 3). The biomarker subgroups NLR > 3 and PLR > 141 demonstrated numerically shorter median OS for tislelizumab versus sorafenib
- A limited difference in median OS was observed between the higher and lower platelet count threshold subgroups (< 2 months), which may indicate a restricted prognostic value for this biomarker (Figure 4)
- The analysis suggests that ALBI grade could have prognostic value for OS, irrespective of treatment
- OS by potential risk factors in the intent-to-treat (ITT) analysis set is shown in Figure 4

Table 1. Baseline Characteristics (ITT Analysis Set)

	TIS (n=342)	SOR (n=332)	Total (N=674)
Age, years, mean (SD)	60.2 (12.5)	59.3 (12.7)	59.8 (12.6)
Male sex, n (%)	289 (84.5)	281 (84.6)	570 (84.6)
ECOG PS 1, n (%)	159 (46.5)	151 (45.5)	310 (46.0)
BCLC Stage, n (%)			
Stage B	70 (20.5)	80 (24.1)	150 (22.3)
Stage C	272 (79.5)	252 (75.9)	524 (77.7)
Hepatitis etiology, n (%)			
HBV	203 (59.4)	206 (62.0)	409 (60.7)
HCV	46 (13.5)	39 (11.7)	85 (12.6)
Uninfected	82 (24.0)	80 (24.1)	162 (24.0)
Child-Pugh class, n (%)			
5	263 (76.9)	248 (74.7)	511 (75.8)
6	77 (22.5)	84 (25.3)	161 (23.9)
ALBI grade ^a , n (%)			
≥ 2	82 (24.0)	98 (29.5)	180 (26.7)
1	256 (74.9)	226 (68.1)	482 (71.5)
Platelet count ^a , n (%)			
$> 150K$	189 (55.3)	189 (56.9)	378 (56.1)
$\leq 150K$	149 (43.6)	135 (40.7)	284 (42.1)
PLR ^a , n (%)			
> 141	131 (38.3)	133 (40.1)	264 (39.2)
≤ 141	207 (60.5)	191 (57.5)	398 (59.1)
NLR ^a , n (%)			
> 3	129 (37.7)	120 (36.1)	249 (36.9)
≤ 3	209 (61.1)	204 (61.4)	413 (61.3)

^aMissing, n (%): TIS: 4 (1.2); SOR: 8 (2.4); Total: 12 (1.8). Abbreviations: ALBI, albumin-bilirubin; BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HBV/HCV, hepatitis B/C virus; ITT, intent-to-treat; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; SD, standard deviation; SOR, sorafenib; TIS, tislelizumab.

Figure 1. OS (ITT Analysis Set; ALBI Grade 1)

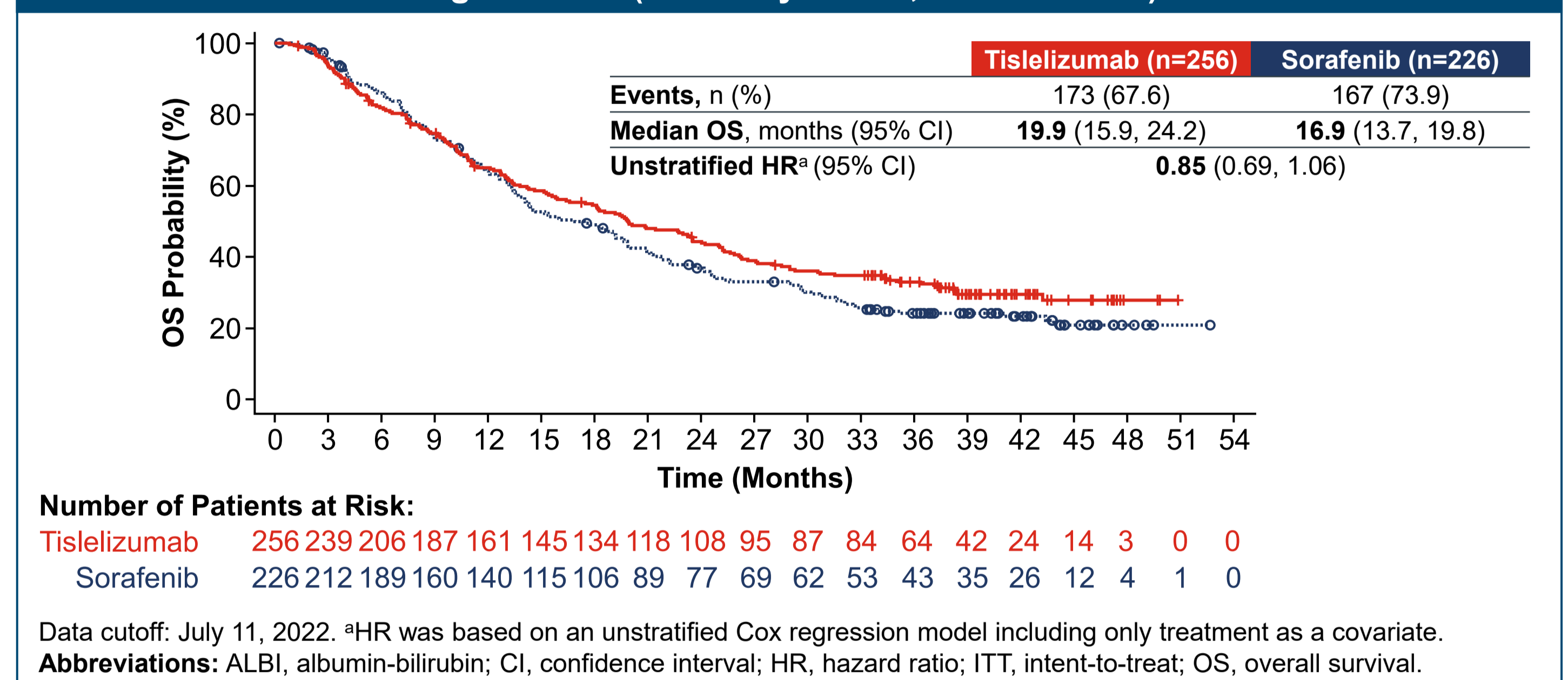


Figure 2. OS (ITT Analysis Set; NLR ≤ 3)

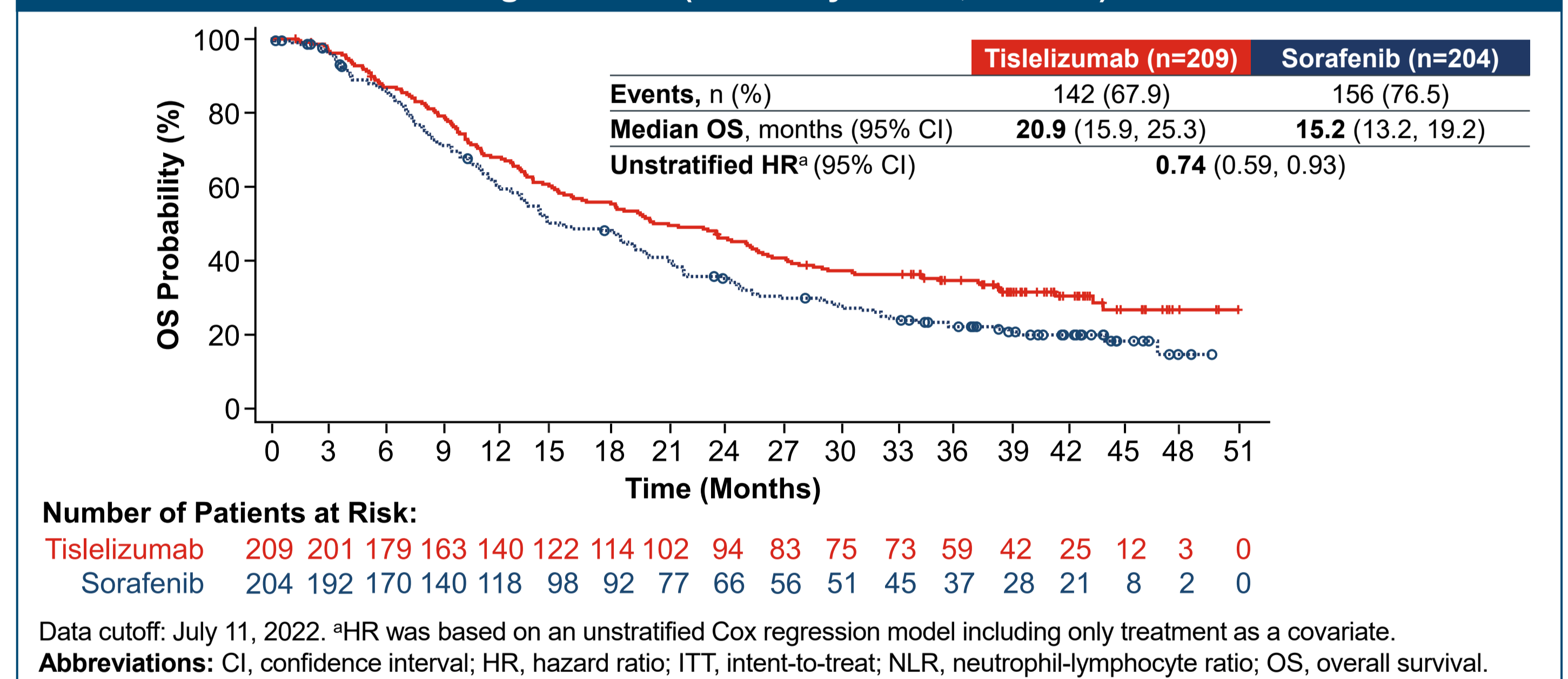


Figure 3. OS (ITT Analysis Set; PLR ≤ 141)

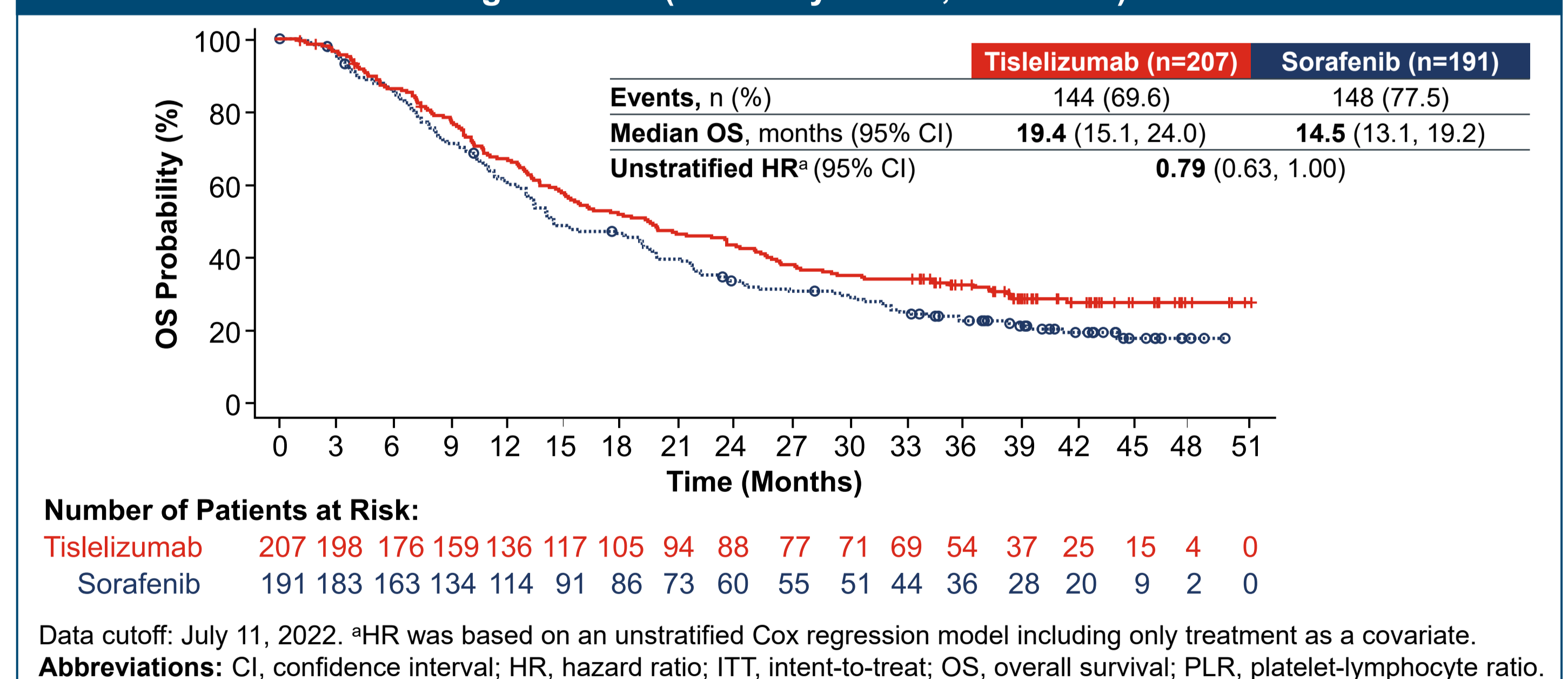
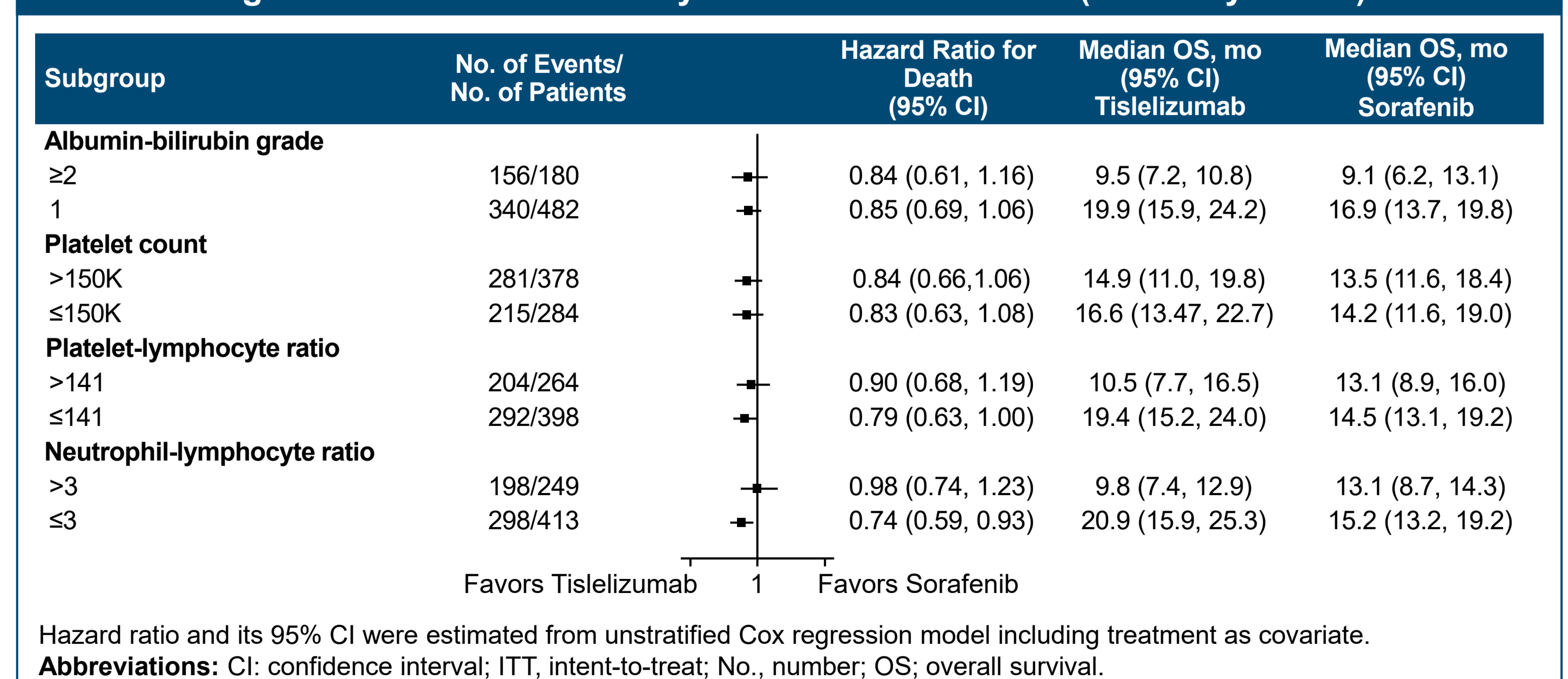


Figure 4. Forest Plot of OS by Potential Risk Factors (ITT Analysis Set)



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