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A DOUBLE-BLIND, RANDOMIZED PHASE 3 STUDY TO COMPARE EFFICACY AND SAFETY OF CT-P10 TO RITUXIMAB IN COMBINATION WITH CVP IN PATIENTS WITH ADVANCED-STAGE FOLLICULAR LYMPHOMA

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Introduction CT-P10 is the first biosimilar of innovator rituximab (RTX), approved for all indications by the EMA. CT-P10 has demonstrated pharmacokinetics (PK) and efficacy equivalence in patients with rheumatoid arthritis (Yoo, ACR 2016) and PK equivalence in patients with advanced follicular lymphoma (AFL) (Coiffier, ASH 2016). This study aimed to demonstrate non-inferiority (NI) of efficacy and PK equivalence between CT-P10 and RTX in patients with newly diagnosed AFL (NCT02162771).

Methods A total of 140 patients were randomized in a 1:1 ratio to receive CT-P10 or RTX (375 mg/m^2 i.v) plus CVP (cyclophosphamide, vincristine and prednisone) every 3 weeks over 8 cycles. Overall response rate (ORR) according to the 1999 IWG criteria based on best overall response over 24 weeks was assessed by the independent review committee.

Results An ORR of 97.0% and 92.6% and a CR/CRu of 39.4% and 33.8% for CT-P10 and RTX, respectively, was observed after 8 cycles of therapy (Table 1). Based on this, the therapeutic NI of CT-P10 to RTX with regard to ORR over 8 cycles was demonstrated as the difference in ORR between the two groups was 4.3% and the lower bound of the two-sided 95% CI was -4.25%. The lower bound (-4.25%) was greater than the pre-defined NI margin (-7%), by this fulfilling the criteria for NI of CT-P10 to RTX.

At a median follow-up of 17 months, 10 patients in the CT-P10 group and 13 patients in the RTX group experienced disease progression or death. There was no statistically significant difference between the

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two groups for PFS (P-value: 0.4802, Log-rank test) although the median PFS survival has not been reached in either arm as a longer follow-up is required (Figure 1).

Median number of B-cells decreased to the lower limit of quantification (LLoQ) after the 1st infusion and remained at the LLoQ over 8 cycles in both groups.

Overall safety profile of CT-P10 was consistent with that of RTX (Table 1) and the proportion of patients with positive anti-drug antibody were similar between the two groups (4.3% and 2.9%) over 24 weeks. No progressive multifocal leukoencephalopathy or Hepatitis B virus reactivation was reported in both groups.

Table 1. Summary of efficacy and safety over 24 weeks treatment

	CT-P10	**RTX**
N (%)	**(N=66)**	**(N=68)**
ORR (CR+CRu+PR)	64 (97.0)	63 (92.6)
Complete response (CR)	20 (30.3)	15 (22.1)
Unconfirmed CR (CRu)	6 (9.1)	8 (11.8)
Partial response (PR)	38 (57.6)	40 (58.8)
	(N=70)	**(N=70)**
TEAE related to the study drug		
Treatment-emergent adverse event (TEAE)*	37 (52.9)	34 (48.6)
Serious TEAE*	6 (8.6)	4 (5.7)
Infusion-related reaction*	15 (21.4)	17 (24.3)
Infection*	6 (8.6)	9 (12.9)

* Difference between groups is not statistically significant.

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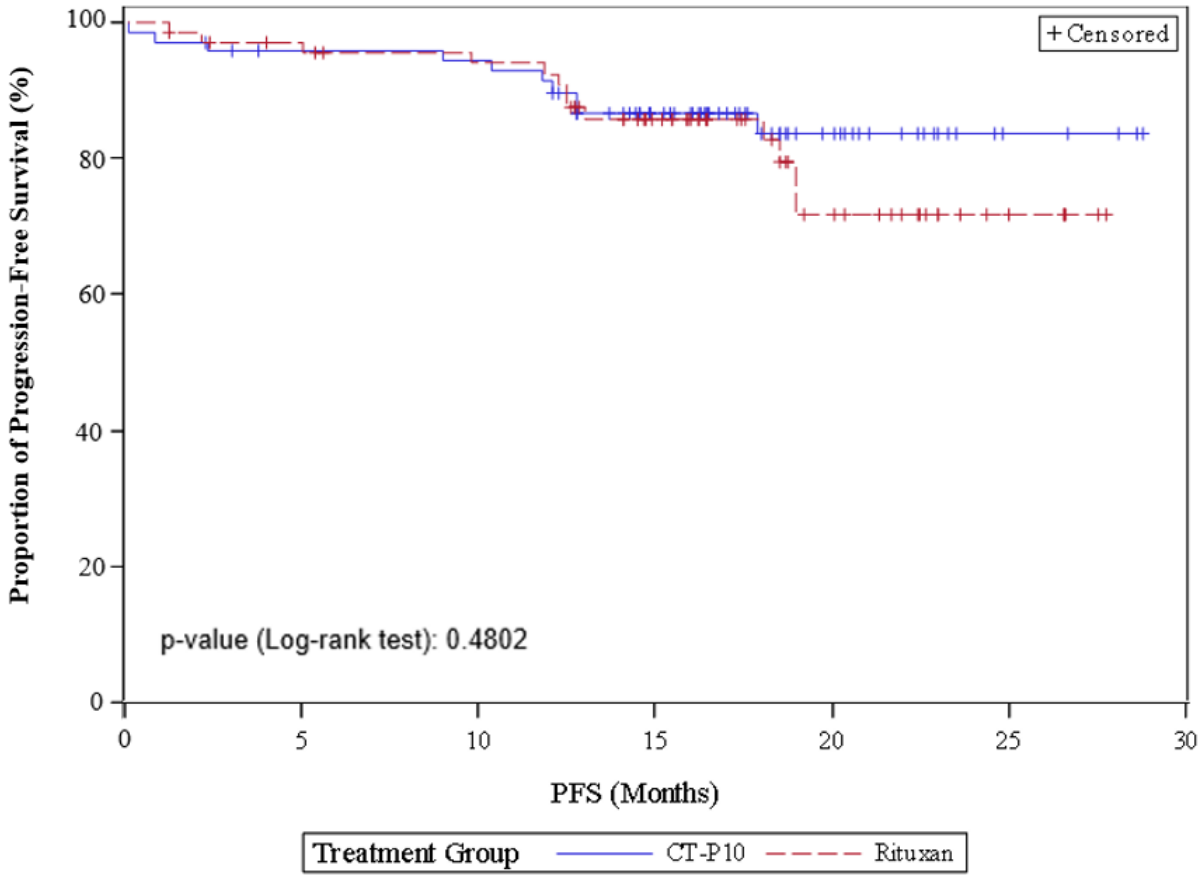
Figure 1. Time to Progression Free Survival (Kaplan-Meier analysis)



Conclusions This study demonstrates therapeutic NI of CT-P10 to RTX plus CVP in previously untreated AFL. CT-P10 was well-tolerated and the safety profile including immunogenicity of CT-P10 was comparable to that of RTX over 8 cycles.