# Efficacy and Safety of CT-P10 Versus Rituximab in Untreated Low-Tumor-Burden Follicular Lymphoma: Final Results of a Randomized Phase III Study

Larry W. Kwak,[1] Juan-Manuel Sancho,[2] Seok-Goo Cho,[3] Hideyuki Nakazawa,[4] Junji Suzumiya,[5] Gayane Tumyan,[6] Jin Seok Kim,[7] Tobias Menne,[8] José Mariz,[9] Nikolai Ilyin,[10] Wojciech Jurczak,[11] Aurelio Lopez Martinez,[12] Olga Samoilova,[13] Edvard Zhavrid,[14] Eduardo Yañez Ruiz,[15] Marek Trneny,[16] Leslie Popplewell,[17] Michinori Ogura,[18] Won-Seog Kim,[19] Sang Joon Lee,[20] Sung Hyun Kim,[20] Keum Young Ahn,[20] Christian Buske[21]

## Abstract

**We assessed the efficacy and safety of rituximab and its biosimilar, CT-P10, in treatment-naïve low-tumor-burden follicular lymphoma patients, with a median follow-up of 29.2 months. Data from the trial show that the efficacy and safety of rituximab and CT-P10 were similar, including after a single switch from rituximab to CT-P10. These data support the therapeutic similarity of rituximab and CT-P10.**

**Introduction:** This double-blind, parallel-group, active-controlled phase III trial (NCT02260804) assessed CT-P10 and rituximab safety and efficacy in patients with previously untreated low-tumor-burden follicular lymphoma (LTBFL), including after a single switch from rituximab to CT-P10. **Patients and Methods:** LTBFL patients were randomized (1:1) to

*Abbreviations:* ADA, antidrug antibody; CI, confidence interval; FL, follicular lymphoma; GELF, Groupe D'Etude des Lymphomes Folliculaires; IRR, infusion-related reaction; ITT, intention-to-treat; IV, intravenously; LTBFL, low-tumor-burden follicular lymphoma; MP1, maintenance period 1; MP2, maintenance period 2; NCCN, National Comprehensive Cancer Network; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RA, rheumatoid arthritis; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event; TTE, time-to-event; TTP, time to progression.

[1]Comprehensive Cancer Center, Duarte, CA 91010
[2]Hematology Department, The Catalan Institute of Oncology—The Josep Carreras Leukemia Research Institute, Hospital Germans Trias i Pujol, Carretera Canyet, Badalona, 08916, Spain
[3]Department of Hematology, Catholic Blood and Marrow Transplantation Center, Seoul St. Mary's Hospital, The Catholic University of Korea, Seoul, 06591, South Korea
[4]Department of Hematology, Shinshu University School of Medicine, Nagano 390-8621, Japan
[5]Shimane University Hospital, Innovative Cancer Center/Oncology-Hematology, Izumo, Shimane 693-8501, Japan
[6]Division of Hematology and Bone Marrow Transplantation, N. N. Blokhin Russian Cancer Research Center, Russian Academy of Medical Science, Moscow, 115478, Russia
[7]Department of Internal Medicine, Yonsei University College of Medicine, Severance Hospital, Seoul, 03722, South Korea
[8]Northern Institute for Cancer Care, Newcastle University, NE7 7DN, UK
[9]Department of Onco-Hematology, Portuguese Institute of Oncology, Rua Dr Antonio Bernardino de Almeida, Porto, 4200-072, Portugal
[10]Russian Research Center for Radiology and Surgical Technologies, Ministry of Health of the Russian Federation, p. Pesochny, 197758, Russia
[11]Maria Sklodowska-Curie National Research Institute of Oncology, 331-115 Kraków, Poland
[12]Department of Hematology, Hospital Arnau de Vilanova, Valencia, Comunidad Valenciana, 46015, Spain
[13]Department of Hematology, Nizhniy Novgorod Region Clinical Hospital, Nizhniy Novgorod, 603126, Russia
[14]N. N. Alexandrov Republican Scientific and Practical Centre of Oncology and Medical Radiology, Lesnoy, Minsk, 223040, Belarus
[15]Department of Internal Medicine, Oncology-Hematology Unit, School of Medicine, Universidad de la Frontera, Temuco, 4780000, Chile
[16]Department of Medicine, Charles University, 128 08, Czech Republic
[17]Toni Stephenson Lymphoma Cancer Center and Department of Hematology and Hematopoietic Cell Transplantation, Duarte, CA 91010
[18]Department of Hematology and Oncology, Kasugai Municipal Hospital, Aichi 486-8510, Japan
[19]Hematology and Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, 06355, South Korea
[20]Celltrion, Inc, Incheon, 22014, South Korea
[21]Institute of Experimental Cancer Research, Comprehensive Cancer Center Ulm, University Hospital of Ulm, 89081 Ulm, Germany

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Address for correspondence: Christian Buske, Institute of Experimental Cancer Research, Comprehensive Cancer Center Ulm, University Hospital of Ulm, Albert-Einstein-Allee 11, 89081 Ulm, Germany
E-mail contact: christian.buske@uni-ulm.de



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receive CT-P10 or rituximab (375 mg/m$^2$ intravenously; day 1 of 4 7-day cycles). Patients achieving disease control entered a 2-year maintenance period. CT-P10 or rituximab were administered every 8 weeks (6 cycles) in year 1; all patients could receive CT-P10 (every 8 weeks; 6 cycles) in year 2. Secondary endpoints (reported here) were overall response rate (ORR) during the study period, progression-free survival (PFS), time to progression (TTP), and overall survival (OS). Safety and immunogenicity were evaluated. **Results:** Between November 9, 2015 and January 4, 2018, 258 patients were randomized (130 for CT-P10; 128 for rituximab). ORR was similar between groups over the study period (CT-P10: 88%; rituximab: 87%). After 29.2 months' median follow-up, median PFS, TTP, and OS were not estimable; 24-month Kaplan-Meier estimates suggested similarity between groups. Overall, 114 (CT-P10: 88%), and 104 (rituximab: 81%) patients experienced treatment-emergent adverse events. The single switch was well tolerated. **Conclusion:** These updated data support therapeutic similarity of CT-P10 and rituximab and support the use of CT-P10 monotherapy for previously untreated LTBFL.

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**Keywords:** Biosimilar, Single switch, Time-to-event data, Therapeutic similarity

## Introduction

Rituximab is an anti–CD20 monoclonal antibody that has shifted the treatment paradigm for follicular lymphoma (FL).[1,2] European Society for Medical Oncology clinical practice guidelines state that rituximab monotherapy can be considered as first-line therapy for the treatment of patients with low-tumor-burden follicular lymphoma (LTBFL) who have mild symptoms.[3] In the United States, National Comprehensive Cancer Network (NCCN) guidelines state that rituximab monotherapy is a recommended regimen that can be considered for the treatment of patients with LTBFL.[4]

CT-P10 (Truxima; Celltrion, Incheon, South Korea) was the first rituximab biosimilar to receive regulatory approval in many countries,[5,6] and NCCN guidelines state that an approved biosimilar is an appropriate substitute for rituximab.[4] Clinical evidence supporting regulatory approval of CT-P10 included studies in patients with FL and rheumatoid arthritis (RA), as discussed in 2 recent articles.[7,8] As with other biosimilars, uptake of CT-P10 has been predicted to lead to significant cost savings, which could contribute to improving access to rituximab treatment.[9] However, only a few studies in patients with RA have assessed whether switching from rituximab to CT-P10 results in any differences with regard to efficacy and safety.[10,11]

The phase III trial reported herein assessed the therapeutic equivalence of single-agent CT-P10 and rituximab in previously untreated patients with LTBFL.[12] Therapeutic equivalence was shown for the primary efficacy endpoint, overall response rate (ORR) over 7 months in the intention-to-treat (ITT) population by central review, as the 2-sided 90% confidence intervals (CIs) (−6.43, 10.20) for the treatment difference estimate (1.8%), calculated using the exact binomial method, were within the predefined equivalence margin of ± 17%.[12] This article reports secondary efficacy outcomes from the study, including ORR, progression-free survival (PFS), time to progression (TTP), and overall survival (OS). In addition, we report updated safety findings for the study period of up to 27 months, including a single switch from rituximab to CT-P10.

## Patients and Methods

### *Study Design, Patients, and Procedures*

This was a double-blind, international, multicenter, phase III study (ClinicalTrials.gov: NCT02260804; EudraCT number: 2014-005324-10) that randomized patients with previously untreated LTBFL at 96 centres. Patients eligible for this study were aged ≥18 years with low tumor burden (per Groupe D'Etude des Lymphomes Folliculaires [GELF] criteria) FL (histologic grade 1, 2, or 3a). The study design and eligibility criteria have previously been described in full.[12]

During the induction period, patients received CT-P10 or US-sourced rituximab (Rituxan; Genentech, South San Francisco, CA) (375 mg/m$^2$ intravenously [IV], diluted to a final concentration of 1-4 mg/mL in normal saline, on day 1 of 4 7-day cycles). Following the induction period, patients with disease control continued to a maintenance period of CT-P10 or rituximab (administered every 8 weeks for 6 cycles [1 year]; MP1); if the initial maintenance period was completed, a second maintenance period (6 cycles [1 year]; MP2) of CT-P10 treatment was provided to all patients at the discretion of the investigator. The initial infusion rate for CT-P10 or rituximab was 100 mg/hour (or 50 mg/hour for cycle 1 of the induction period), which was increased in increments of 100 mg/hour (or 50 mg/hour for cycle 1 of the induction period) every 30 minutes to a maximum rate of 400 mg/hour in the absence of infusion toxicity. Antipyretic (oral paracetamol 500 mg), antihistamine (H1 antihistamine [oral or IV]) and prednisone (oral or IV 40 mg/m$^2$) premedication was administered 30 minutes before each study drug infusion throughout the study. In addition, any medications that were appropriate and part of the study center practice, including antiemetics, hydration, or antacids, could be administered as premedication. Following MP2, patients entered a follow-up period during which they were monitored every 6 months (± 2 weeks) for disease status until treatment with a new anticancer therapy or disease progression, and every 3 months (± 2 weeks) for survival and salvage treatment until death or study termination (up to 27 months from the first visit of the final enrolled patient).

Tumor response was assessed at baseline and months 3, 7, 13, 19, and 27, and then every 6 months during the follow-up period using the modified response criteria for malignant lymphoma on the basis of the International Working Group response criteria.[13] Overall safety and immunogenicity were also evaluated.[12]

The study was conducted in accordance with the Declaration of Helsinki, the protocol was approved by ethics committees at each center, and all patients provided written informed consent.[12]

### *Outcomes*

The secondary objectives of the study were to evaluate ORR during the study period, PFS, TTP, and OS. ORR was defined as the proportion of patients whose best overall response was complete response, unconfirmed complete response, or partial response. Time-to-event (TTE) parameters were defined per Cheson *et al.*[14] In addition to the secondary efficacy objectives, safety, and immunogenicity were evaluated throughout the study period.

### *Statistical Analyses*

Details regarding the sample size and analysis populations have been previously reported.[12] ORR during the study period by central and local review was summarized by treatment group in the ITT and per-protocol populations. TTE analyses were performed by the Kaplan-Meier method for PFS, TTP, and OS analyses (by local review) in the ITT population. Median time and survival rates per 6 months (with corresponding 95% CIs) were estimated using the Kaplan-Meier method. OS, PFS, TTP, and follow-up duration were analyzed with data including the follow-up period. Safety endpoints were summarized by treatment group in the safety population.

## Results

Patients were assessed for eligibility between November 9, 2015 and January 4, 2018,[12] and the date of the last follow-up visit was September 4, 2019. Overall, 402 patients were screened, and 258 patients were randomized and initiated treatment with CT-P10 ($n=130$) or rituximab ($n=128$) (Figure 1). The majority of patients (198 [77%]) completed all 12 planned maintenance cycles, including 97 patients who underwent a single switch from reference rituximab to CT-P10. As previously reported, baseline patient demographics, and disease characteristics were balanced between groups.[12]

The ORR was similar between groups, with overall response achieved by 88% and 87% patients in the CT-P10 and rituximab groups, respectively (central review), and 84% and 88% patients, correspondingly, by local review (Table 1). There was high concordance in ORR between data reviewed by central and local reviewers (Supplemental Table 1). Concordant rates were found for 88% and 95% in the CT-P10 and rituximab groups, respectively. Among evaluable patients, ORR by central review at each visit was highly similar between groups (Supplemental Table 2).

As all patients received CT-P10 in the second year of the maintenance period, efficacy was also evaluated following a single switch from reference rituximab to CT-P10, and compared with findings for patients who received CT-P10 throughout the study period. Results for months 19 and 27 reflect efficacy after the single switch in the rituximab group. Similar proportions of patients in each treatment group achieved overall response at month 27 (97% for CT-P10 throughout and 94% for the single switch to CT-P10). The ORR gradually increased and remained similar by visit even after the single switch. By local review, ORR was also similar between groups across study visits (Supplemental Table 3).

**Table 1** Response Rates for the Study Period, by Central and Local Review (ITT Population)

| | CT-P10 ($n=130$) | Rituximab ($n=128$) |
|---|---|---|
| Central review | | |
| Overall response | 115 (88) | 111 (87) |
| Complete response | 73 (56) | 66 (52) |
| Unconfirmed complete response | 4 (3) | 6 (5) |
| Partial response | 38 (29) | 39 (30) |
| Stable disease | 10 (8) | 11 (9) |
| Relapsed disease or progressive disease | 0 | 4 (3) |
| Unable to assess[a] | 0 | 1 (1) |
| Data missing[b] | 5 (4) | 1 (1) |
| Local review | | |
| Overall response | 109 (84) | 112 (88) |
| Complete response | 51 (39) | 63 (49) |
| Unconfirmed complete response | 7 (5) | 2 (2) |
| Partial response | 51 (39) | 47 (37) |
| Stable disease | 15 (12) | 12 (9) |
| Relapsed disease or progressive disease | 1 (1) | 3 (2) |
| Unable to assess[a] | 0 | 0 |
| Data missing[b] | 5 (4) | 1 (1) |

Data are n/N (%).
Abbreviation: ITT = intention-to-treat.
[a] Patient had incomplete target lesion assessment.
[b] Patients who discontinued treatment early without tumor response evaluation at post-treatment visits.

In the ITT population, the Kaplan-Meier estimates (95% CI) for OS at 24 months were 98% (93-99) and 98% (94-100) in the CT-P10 and rituximab groups, respectively. Corresponding values for PFS were 88% (81-92) and 83% (75-89), while results for TTP were 89% (82-94) and 84% (76-89) in the CT-P10 and rituximab groups, respectively. At a median follow-up of 29.2 months (interquartile range 26.1-33.7), median OS (Figure 2A), PFS (Figure 2B), and TTP (Figure 2C) were not reached; this is likely due to the low number of events of disease progression, relapse, or death during the study period. Kaplan-Meier estimates showed that TTE results before the single switch (at 6 and 12 months) were in line with those after the single switch (at 24 months).

Over the study period, 114 (88%) and 104 (81%) patients in the CT-P10 and rituximab groups, respectively, experienced at least 1 treatment-emergent adverse event (TEAE) (Table 2). Most TEAEs were grade 1-2 in intensity. Overall, similar proportions of patients experienced at least 1 TEAE of infection or infusion-related reaction (IRR) in each group (Table 2). In the CT-P10 group, 99 TEAEs of infection occurred in 59 patients, while 113 TEAEs of infection occurred in 53 patients treated with rituximab. All IRRs were grade 1-2 in intensity, except for 1 grade

**Figure 1** Trial profile. Abbreviation: ITT = intention-to-treat. [a]Two patients had insurance problems, 12 patients were out of the screening window, and adequate equipment was not prepared for the study for 1 patient (no computed tomography). [b]Discontinued treatment to receive prohibited treatment. [c]All patients in the rituximab arm who completed the first year of the maintenance period underwent a single switch to CT-P10 and received CT-P10 throughout the second year of the maintenance period.

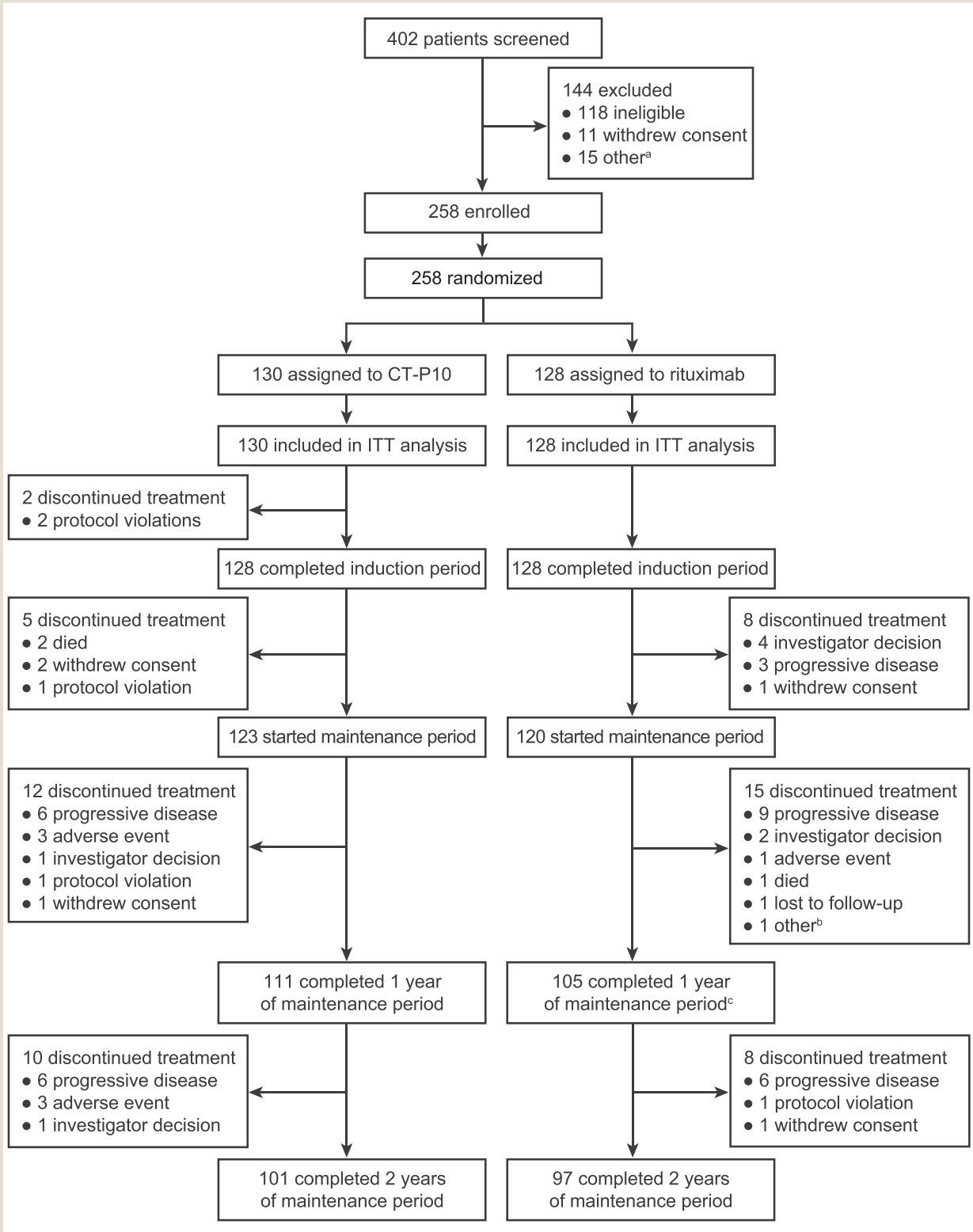

**Figure 2** Kaplan-Meier curves for time-to-event analyses (Intention-to-treat population). (A) OS. (B) PFS. (C) TTP. Abbreviations: NE = not estimable; OS = overall survival; PFS = progression-free survival; TTP = time to progression.

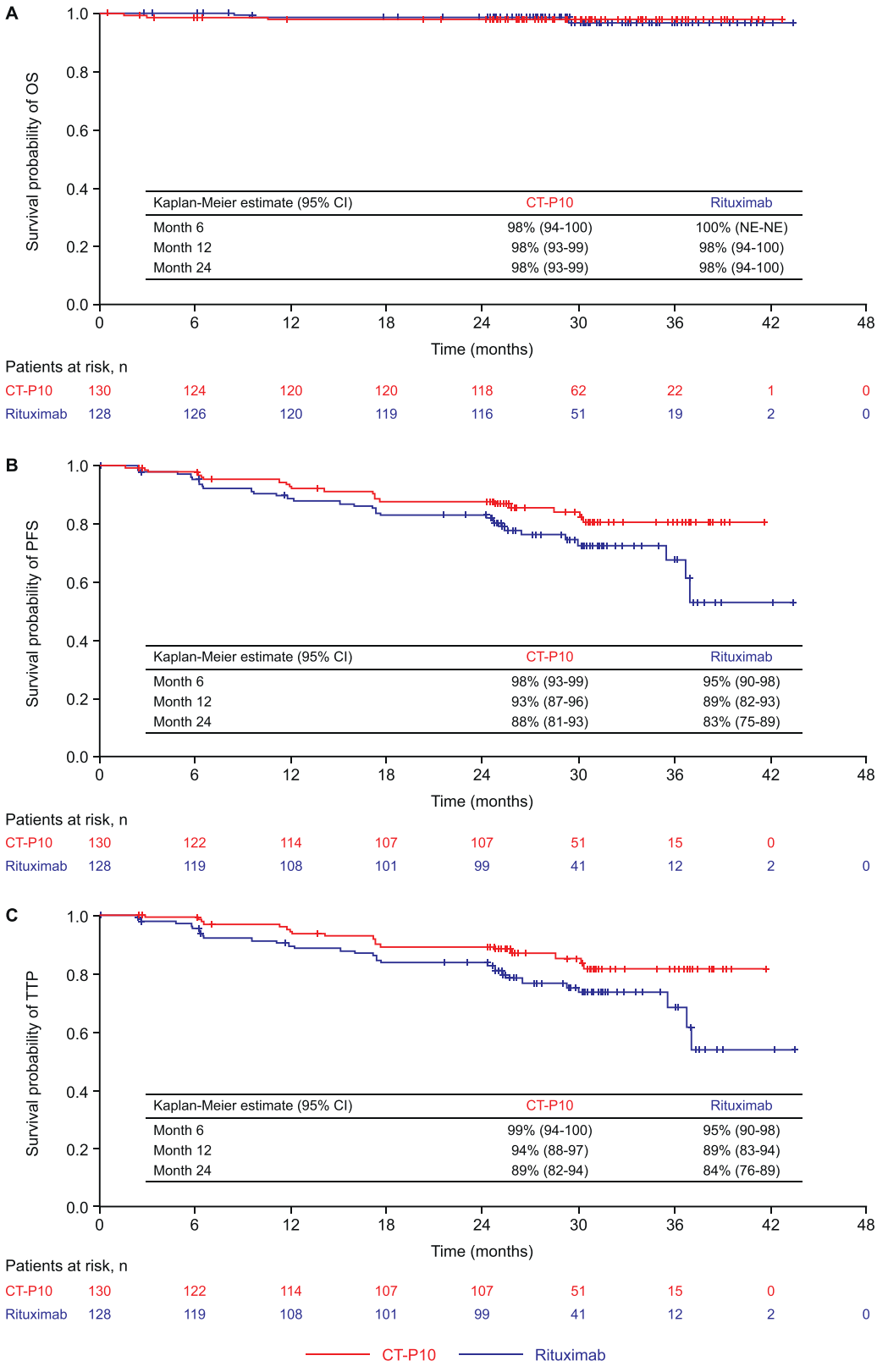

**Table 2** Summary of TEAEs During the Study Period (Safety Population).

| | CT-P10 ($n = 130$) | Rituximab ($n = 128$) |
|---|---|---|
| Total number of TEAEs | 593 | 591 |
| Patients with ≥ 1 TEAE | 114 (88) | 104 (81) |
| Study drug-related | 74 (57) | 64 (50) |
| Patients with ≥ 1 TEAE due to infections and infestations | 59 (45) | 53 (41) |
| Study drug-related | 21 (16) | 15 (12) |
| Patients with ≥ 1 TEAE leading to permanent study drug discontinuation | 9 (7) | 2 (2) |
| Study drug-related | 3 (2) | 2 (2) |
| Patients with ≥ 1 TEAE due to IRRs | 42 (32) | 39 (30) |
| Patients with ≥ 1 TEAE due to PML | 0 | 0 |
| Patients with ≥ 1 TESAE | 14 (11) | 14 (11) |
| Study drug-related | 3 (2) | 4 (3) |
| TEAE ≥ 5% patients in either treatment group | | |
| Abdominal pain | 6 (5) | 7 (5) |
| Alanine aminotransferase increased | 7 (5) | 3 (2) |
| Back pain | 8 (6) | 5 (4) |
| Cough | 9 (7) | 12 (9) |
| Diarrhoea | 9 (7) | 11 (9) |
| Fatigue | 10 (8) | 13 (10) |
| Headache | 6 (5) | 7 (5) |
| Herpes virus infection | 7 (5) | 5 (4) |
| Hypertension | 10 (8) | 6 (5) |
| Influenza | 3 (2) | 8 (6) |
| IRR | 42 (32) | 39 (30) |
| Lower respiratory tract infection | 6 (5) | 11 (9) |
| Nausea | 7 (5) | 11 (9) |
| Neutropenia | 10 (8) | 7 (5) |
| Upper respiratory tract infection | 31 (24) | 29 (23) |
| Urinary tract infection | 9 (7) | 14 (11) |
| Worsening haematological events by laboratory assessment[a] | | |
| Anaemia | 21 (16) | 23 (18) |
| Haemoglobin increased | 9 (7) | 14 (11) |
| Neutrophil count decreased | 42 (32) | 39 (30) |
| Platelet count decreased | 12 (9) | 14 (11) |
| White blood cell count decreased | 36 (28) | 45 (35) |

Data are number of patients (%).
Abbreviations: IRR = infusion-related reaction; PML = progressive multifocal leukoencephalopathy; TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event.
[a] Worsened Common Terminology Criteria for Adverse Events grades compared with baseline.

3 IRR previously reported in the CT-P10 group.[12] This IRR occurred at cycle 1 of the induction period and resolved within 2 hours; the patient reported no further IRRs. There were no cases of progressive multifocal leukoencephalopathy. During the study period, 14 (11%) patients in each group experienced treatment-emergent serious adverse events (TESAEs) (Table 2). Study drug-related TESAEs were experienced by 3 (2%) and 4 (3%) patients in the CT-P10 group and rituximab groups, respectively (Supplemental Table 4). During MP2, no clinically meaningful differences were found between the groups (Supplemental Table 5) and there were no new or unexpected safety findings observed during MP2, compared with the data up to MP1 (Supplemental Table 5 vs. Supplemental Table 6).

Six deaths were reported during the study period, including 3 due to TEAEs. As previously reported, 2 patients in the CT-P10 group died due to TEAEs occurring during the induction period (myocardial infarction and respiratory failure).[12] One patient in the rituximab group died during MP1 due to pneumonia considered possibly related to study drug. There were 3 deaths due to lymphoma during the follow-up period: 2 patients in the rituximab group and 1 in the CT-P10 group.

Throughout the study, only a minority of patients (1 [< 1%] for CT-P10 and 3 [2%] for rituximab) tested positive for antidrug antibodies (ADAs).[12] No further patients reported positive ADA or neutralizing antibody results during the study after month 7, including patients who underwent the single switch.

## Discussion

Our study provides an insight into the efficacy and safety of rituximab biosimilar CT-P10 and rituximab treatment in LTBFL, with up to 27 months of follow-up. The design of MP2 also allowed us to evaluate the efficacy and safety of a single switch from rituximab to CT-P10, which is the key strength of this study. As anticipated, the ORR was higher for the overall study period (88% for CT-P10; 87% for rituximab), compared with the primary analysis at month 7 (83% for CT-P10; 81% for rituximab).[12] Safety profiles across the study period were comparable between groups, and no new safety signals were detected, including after the single switch. The results reported here indicate the therapeutic similarity of CT-P10 and rituximab, supporting the therapeutic equivalence of the 2 drugs demonstrated for the primary endpoint of the study.[12]

As far as we are aware, only 1 other study to date has evaluated single-agent rituximab in patients with LTBFL using the same regimen and treatment schedule as our study.[15] In the ITT population, the ORR in our study was 88% (CT-P10) and 87% (rituximab) over 27 months by central review; by local review, ORR was 84% (CT-P10) and 88% (rituximab). The ORR in our study is similar to the ORR at 25 months of 83% among the patients receiving maintenance rituximab therapy in Ardeshna *et al.*[15] We also determined response rates among evaluable patients at each study visit, with findings comparable to the rates identified in the Ardeshna *et al* study.[15] At month 7, the ORR was 89% in the CT-P10 group and 83% in the rituximab group by central review; corresponding values were 81% and 79% by local review. Similarly, the ORR at month 13 was 88% in the CT-P10 group and 90% in the rituximab group (by central review; 85% and 88%, correspondingly, by local review), which is comparable to the 89% ORR previously reported by Ardeshna *et al.*[15] Taken together, these results support the comparability in efficacy of CT-P10 and rituximab in single-agent therapy for LTBFL.

Concordance between central and local review in our study was high. This indicates that the tumor assessment in our study, based on the modified response criteria for malignant lymphoma,[13] was accurate, and reproducible.

Single-agent rituximab induction therapy has been evaluated in patients with LTBFL, using the same induction regimen as we implemented. In the RESORT trial, 289/408 patients (71%; 95% CI 67-76) responded to rituximab induction therapy (4 weeks).[16] A comparable ORR (73%) was reported among 49 patients following rituximab induction treatment (day 50).[17] These response rates are similar to our results for the first study visit of the maintenance period (month 3), when the ORR among evaluable patients was 65% and 71% in the CT-P10 and rituximab groups, respectively (by central review). Another recently reported study compared induction therapy with the rituximab biosimilar PF-05280586 and EU-sourced rituximab.[18] Among patients evaluable by central review at week 26, respective ORRs were 85% and 76%.[18] These are comparable to the ORRs of 89% and 83% reported at month 7 in our study for patients evaluable by central review in the CT-P10 and rituximab groups, respectively. However, comparisons with previous reports should be made cautiously because results were assessed at different time points and the denominators used for determining response rates may differ.

Although median OS, PFS, and TTP were not reached in our study, this may have been due to the relatively low proportion of death or disease progression or relapse events occurring in this indolent disease. Therefore, numerical differences between treatment groups in our study, in terms of the TTE endpoints, should be interpreted with caution in view of a relatively immature dataset. Also, it is important to note the lack of statistical power to formally assess the secondary endpoints.[12] Furthermore, there were no significant differences in OS, PFS, and TTP in a phase III study evaluating CT-P10 and rituximab in patients with advanced FL.[19]

The proportion of patients experiencing TEAEs was comparable between the CT-P10 and rituximab groups, for the study period, before and after the single switch. In addition, the total number of TEAEs for each period was similar between treatment groups. We found that infections occurred at a similar frequency to that reported in the rituximab product information for registrational trials in patients with non–Hodgkin lymphoma. Infections were experienced by 45% of patients in the CT-P10 group and 41% of patients in the rituximab group, compared with 30%-55% of patients in the rituximab registrational studies.[5] IRRs occurred at a lower frequency in our study than in rituximab registrational studies (32% CT-P10 and 30% rituximab vs. > 50%).[5] During the study period, the proportion of patients with at least 1 TEAE was slightly higher in the CT-P10 group than the rituximab group (88% vs. 81%). However, during the study period, the numerical difference between the total numbers of TEAEs experienced by each treatment group was minimal (593 events for CT-P10; 591 events for rituximab). The proportion of patients experiencing TEAEs leading to permanent study drug discontinuation was also numerically higher in the CT-P10 group than the rituximab group (7% vs. 2%), although the proportions for study drug-related events were identical between treatment groups (2% for both CT-P10 and rituximab groups).

The low incidence of immunogenicity throughout our study is in keeping with findings reported up to month 7.[12] It is also similar to the 1% of patients with low-grade or follicular non–Hodgkin lymphoma who developed ADAs following rituximab treatment, and within the range of the frequency of ADA-positive patients (1%-56%) reported across indications in rituximab registrational trials.[20,21]

The uptake of biosimilars in oncology has the potential to deliver cost savings for healthcare systems, potentially expanding patient access to biologic treatments.[9] However, physicians may have concerns regarding safety and efficacy when switching a patient from reference biologic to biosimilar.[22] Furthermore, a recent review concluded that additional clinical data are required to guide switching decisions in the oncology setting.[23]

Our study evaluated the efficacy and safety of a single switch from rituximab to CT-P10, with all patients who had been receiving rituximab switched to CT-P10 on entering MP2. When considering findings for study visits after the single switch as a whole, ORR was similar between the groups of patients who received CT-P10 throughout and those who underwent the single switch. In addition, data from a Korean post-marketing surveillance study

have identified that 96% of patients with FL, who had been treated with rituximab before study participation, experienced improved or maintained response even after switching to CT-P10 (S.J.L. and S.H.K., unpublished data, November 15, 2020). In a retrospective real-world analysis of first-line diffuse large B-cell lymphoma treatment, there were no significant differences in efficacy outcomes for patients who received rituximab throughout, CT-P10 throughout, or switched from rituximab to CT-P10 during their treatment.[24] Taken together, these data provide further evidence to support the finding that a single switch from rituximab to CT-P10 does not impact efficacy.

Safety results showed that there were no new or unexpected safety signals following the single switch. There was no increase in the incidence of TEAEs, which were reported by 73% of patients in the rituximab group up to the end of MP1, and 69% of patients during MP2 after the single switch. In addition, there was no new development of ADAs after the single switch. The overall similarity in safety and efficacy profiles between these groups is in line with previous data from studies evaluating switching to CT-P10 in RA patients. In a phase 1 study, safety and efficacy were comparable for patients with RA who switched from rituximab to CT-P10 and those who received CT-P10 throughout.[10] Safety, efficacy, pharmacodynamics and immunogenicity were also comparable between patients with RA continuing to receive CT-P10 or US-sourced reference rituximab or switching from EU- or US-sourced reference rituximab to CT-P10 in a phase III trial.[11]

## Conclusion

These data provide an update on the efficacy and safety of CT-P10 and rituximab treatment in LTBFL, with up to 27 months of follow-up. They support the therapeutic similarity of CT-P10 and rituximab in single-agent treatment for previously untreated LTBFL. In addition, the exploratory comparison of efficacy and safety profiles between patients who received CT-P10 throughout or underwent a single switch from rituximab to CT-P10 demonstrates that switching to CT-P10 was well tolerated without loss of efficacy and without raising safety concerns, including those related to immunogenicity. Furthermore, this study provides access to urgently needed data about switching to biosimilars in the oncology setting. Taken together, these data provide support for the role of CT-P10 as a treatment option for LTBFL that could help to deliver cost savings for healthcare systems.

### *Clinical Practice Points*

1. To the best of our knowledge, this study is the first report of long-term efficacy data from a phase III clinical trial of a rituximab biosimilar given as monotherapy for up to 2 years of maintenance treatment in patients with LTBFL.
2. It also presents findings from the largest prospective cohort available to date of newly diagnosed patients with LTBFL treated with rituximab monotherapy.
3. Updated safety data and time-to-event analyses support the comparability in safety profile and equivalence in efficacy between CT-P10 and reference rituximab, adding to the accumulating evidence for the bioequivalence of the 2 drugs.
4. Furthermore, a single switch from reference rituximab to CT-P10 after 1 year of maintenance therapy was well tolerated, with no clinically significant differences identified in terms of efficacy, safety, and immunogenicity. This supports the efficacy and safety of a single switch from reference rituximab to CT-P10.
5. Rituximab biosimilars, especially those with data supporting the safety and efficacy of a single switch from the reference product in multiple indications, represent therapeutic options with the potential to facilitate cost savings and increase access to effective biologic therapies.

## CRediT Authorship Contribution Statement

**Larry W. Kwak:** conceptualization; formal analysis; investigation; methodology; writing - original draft; writing - review & editing. **Juan-Manuel Sancho:** data curation; writing - review & editing. **Seok-Goo Cho:** data curation; writing - review & editing. **Hideyuki Nakazawa:** data curation; writing - review & editing. **Junji Suzumiya:** data curation; writing - review & editing. **Gayane Tumyan:** data curation; writing - review & editing. **Jin Seok Kim:** data curation; writing - review & editing. **Tobias Menne:** data curation; writing - review & editing. **José Mariz:** data curation; writing - review & editing. **Nikolai Ilyin:** data curation; writing - review & editing. **Wojciech Jurczak:** data curation; writing - review & editing. **Aurelio Lopez Martinez:** data curation; writing - review & editing. **Olga Samoilova:** data curation; writing - review & editing. **Edvard Zhavrid:** data curation; writing - review & editing. **Eduardo Yañez Ruiz:** data curation; writing - review & editing. **Marek Trneny:** data curation; writing - review & editing. **Leslie Popplewell:** data curation; writing - review & editing. **Michinori Ogura:** conceptualization; formal analysis; investigation; methodology; writing - review & editing. **Won-Seog Kim:** conceptualization; formal analysis; investigation; methodology; writing - review & editing. **Sang Joon Lee:** conceptualization; formal analysis; investigation; methodology; writing - review & editing. **Sung Hyun Kim:** conceptualization; formal analysis; investigation; methodology; writing - review & editing. **Keum Young Ahn:** conceptualization; formal analysis; investigation; methodology; writing - review & editing. **Christian Buske:** conceptualization; formal analysis; investigation; methodology; writing - original draft; writing - review & editing. All authors had access to the complete clinical data set, reviewed drafts of the manuscript, and approved the final version.

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## Disclosure

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.clml.2021.08.005.

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