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S245 RUXOLITINIB IN PEDIATRIC PATIENTS WITH TREATMENT-*NAIVE* OR STEROID-REFRACTORY CHRONIC GRAFT VERSUS HOST DISEASE: PRIMARY FINDINGS FROM THE PHASE II REACH5 STUDY

Topic: SCT clinical

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Background:

Chronic graft-versus-host disease (cGvHD) is a major complication of allogeneic stem cell transplantation and ≈ 50% of patients (pts) become steroid-refractory (SR) or steroid-dependent. In the phase 3 REACH3 randomized study (Zeiser et al., N Engl J Med, 2021), ruxolitinib (RUX) demonstrated a superior overall response rate (ORR) vs. best available therapy in pts ≥12 years with SR cGvHD.

Aims:

We present the first data from REACH5 (NCT03774082), a phase 2 open-label, single-arm, multicenter study of RUX added to corticosteroids (CS) in pediatric pts with moderate to severe cGvHD.

Methods:

Pts with moderate to severe treatment-*naive* or SR cGvHD were grouped according to age (Group 1: ≥12 to <18 years, Group 2: ≥6 to <12 years, and Group 3: ≥2 to <6 years). All pts received RUX plus CS ± calcineurin inhibitor for up to 3 years (39 cycles of 28 days/week 156); RUX starting dose was 10 mg twice daily [BID] in Group 1, 5 mg BID in Group 2, and 4 mg/m^2 BID in Group 3). The primary efficacy endpoint was ORR at cycle 7 day 1 (C7D1); key secondary endpoints included best overall response (BOR) up to C7D1, failure-free survival, overall survival, and evaluation of safety. CS taper was permitted 2 weeks after the achievement of complete or partial response; following successful CS taper, RUX taper could commence after C7D1. Data were analyzed once all pts had completed 1 year of treatment or discontinued earlier (data cut-off 19 October 2022).

Results:

Overall, 45 pediatric pts were treated with RUX; 64.4% were male and the median age was 11.0 years (range,

2.0–17.8). At screening, 37.8% of pts had moderate cGvHD and 62.2% had severe cGvHD; 62.2% were SR and 37.8% were treatment-*naive*. Median time from cGvHD diagnosis to start of study treatment was 49 days (range,1–2999). At data cut-off, the treatment phase was ongoing for 15 pts and 30 pts had discontinued treatment; the most common reasons for discontinuation were physician's decision (15.6%), adverse event (AE; 13.3%) and lack of efficacy (13.3%).

Among all pts, the ORR at C7D1 was 40% (18/45; 90% confidence interval [CI] 27.7, 53.3) and the BOR rate up to C7D1 was 82.2% (37/45; 90% CI 70.2, 90.8) (Table). ORR at C7D1 in treatment-*naive* and SR pts were 41.2% and 39.3%, respectively. Of pts receiving CS at baseline (40/45; 88.9%), 42.5% (17/40) stopped or completely tapered CS and 75.0% (30/40) had a ≥50% reduction from baseline at least once by C7D1. Among all pts, the CS-free ORR at data cut-off was 37.8% (17/45; 90% CI 25.7, 51.1).

The median duration of RUX exposure was 55.1 weeks (range 2.1–112.1). In total, 97.8% (44/45) of pts had an AE (any grade) and 64.4% had a ≥3 grade AE. Most frequently reported AEs were anemia (22.2% any grade; 20.0% ≥3 grade), COVID-19 (17.8% any grade; 4.4% ≥3 grade) and decreased neutrophil count (17.8% any grade; 17.8% ≥3 grade). Overall, 73.3% (33/45) of pts had an infection. Viral infections occurred in 40.0% (18/45) of pts, including 17.8% (8/45) SARS-CoV-2 infections; bacterial and fungal infections occurred in 2.2% and 11.1% of pts, respectively. Overall, 10 (22.2%) pts died during the study. Three (6.7%) pts died whilst receiving RUX or within 30 days of the last study dose; causes of death were aspergillus pneumonia, septic shock and acute respiratory distress syndrome (1 pt each).

Summary/Conclusion:

In pediatric pts with cGvHD, RUX treatment led to high ORR at C7D1 and a high BOR up to C7D1, across age groups. ORR was similar in treatment-*naive* and SR pts at C7D1. The safety profile was consistent with expectations for RUX and this pt population.

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Table. Summary of the efficacy of ruxolitinib in REACH5 at C7D1

	Group 1 ≥12 to <18yrs N=22	Group 2 ≥6 to <12yrs N=16	Group 3 ≥2 to <6yrs N=7	Treatment-*naive* N=17	Steroid-refractory N=28	All patients N=45
ORR at C7D1, n (%)	8 (36.4)	8 (50.0)	2 (28.6)	7 (41.2)	11 (39.3)	18 (40.0)
90% CI	19.6, 56.1	27.9, 72.1	5.3, 65.9	21.2, 63.6	23.8, 56.5	27.7, 53.3
Responders at C7D1, n (%)						
CR	1 (4.5)	2 (12.5)	1 (14.3)	2 (11.8)	2 (7.1)	4 (8.9)
PR	7 (31.8)	6 (37.5)	1 (14.3)	5 (29.4)	9 (32.1)	14 (31.1)
BOR up to C7D1, n (%)	18 (81.8)	13 (81.3)	6 (85.7)	-	-	37 (82.2)
90% CI	63.1, 93.5	58.3, 94.7	47.9, 99.3	-	-	70.2, 90.8
Responders up to C7D1, n (%)						
CR	2 (9.1)	3 (18.8)	1 (14.3)	-	-	6 (13.3)
PR	16 (72.7)	10 (62.5)	5 (71.4)	-	-	31 (68.9)

Full analysis set. Efficacy was analyzed once all patients had completed 1 year of treatment or discontinued earlier (data cut-off 19 October 2022).

ORR is defined as the proportion of patients demonstrating a CR or PR according to NIH consensus criteria (Lee et al., Biol Blood Marrow Transplant, 2015).

BOR is defined as the proportion of patients who achieved overall response (CR or PR) at any time point up to and including C7D1. BOR has not been evaluated for treatment-*naive* or steroid-refractory subgroups.

The two-sided 90% CI for the response rate was calculated using Clopper Pearson exact method.

BOR, best overall response; C7D1, cycle 7 day 1; CI, confidence interval; CR, complete response; NIH, National Institutes of Health; ORR, overall response rate; PR, partial response