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P1389 RUXOLITINIB DEMONSTRATES A GREATER CORTICOSTEROID-SPARING EFFECT THAN BEST AVAILABLE THERAPY IN PATIENTS WITH CORTICOSTEROID-REFRACTORY/DEPENDENT CHRONIC GRAFT-VS-HOST DISEASE

Topic: 22. Stem cell transplantation - Clinical

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Background: Chronic graft-vs-host disease (cGVHD) is a major complication in recipients of allogeneic stem cell transplants. The recommended treatment for moderate/severe cGVHD is systemic corticosteroids (CS) ± calcineurin inhibitor (CNI). However, limiting exposure to CS is advised due to high morbidity and poor quality of life associated with CS treatment. Additionally, ≈50% of patients (pts) become CS refractory/dependent (SR/D), requiring second-line treatment. Ruxolitinib (RUX), a JAK1/2 inhibitor, demonstrated superior efficacy over best available therapy (BAT) in the phase 3 REACH3 study (NCT03112603) in pts with SR/D cGVHD (Zeiser NEJM 2021).

Aims: To evaluate the impact of RUX vs BAT on CS use in pts with SR/D cGVHD in REACH3.

Methods: Pts aged ≥12 years with moderate or severe SR/D cGVHD were randomized 1:1 to receive either RUX 10 mg twice daily (n=165) or investigator-selected BAT (n=164). Pts received randomized treatment along with CS (prednisone or equivalent) ± CNI for 24 weeks. In this post hoc, descriptive analysis, data were collected from baseline (BL) to week 24, and changes in CS use over time were analyzed by treatment and best overall response (BOR; responders [complete or partial response by 2014 NIH criteria at any time] vs nonresponders).

Results: BL pt characteristics, including body mass index (BMI) and CS dose, were generally balanced between groups—median BMI (RUX vs BAT): responders, 22.7 vs 23.3; nonresponders, 22.4 vs 22.1; median CS dose (mg/day, RUX vs BAT): responders, 30.0 vs 30.0; nonresponders, 33.9 vs 35.0. A greater proportion of RUX vs BAT responders had severe disease (56.3% [71/126] vs 44.4% [44/99]). Overall, median CS dose decreased over time in the RUX and BAT arms and was similar between groups. RUX-treated pts experienced a faster and greater median percentage decrease from BL in CS dose over time vs BAT-treated pts. When analyzed by BOR, the median percentage change (decrease) from BL in CS dose was similar in RUX and BAT responders but was smaller in BAT vs RUX nonresponders (Figure). RUX responders had the greatest median percentage decrease in CS dose over time.

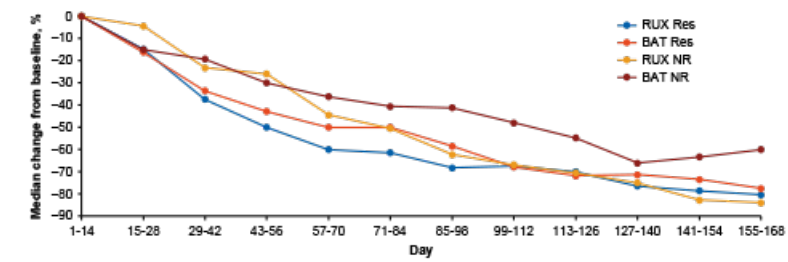
The proportion of pts achieving a ≥50% reduction from BL in CS dose at any time was similar in the RUX and BAT arms (81.2% [134/165] vs 79.9% [131/164]) and RUX and BAT responders (81.7% [103/126] vs 86.9% [86/99]). This proportion was numerically lower in BAT vs RUX nonresponders (69.2% [45/65] vs 79.5% [31/39]). Pts in the RUX arm achieved a ≥50% reduction in CS dose earlier than pts in the BAT arm, with a median time of 1.9 months (95%

CI, 1.4-1.9 months) vs 2.4 months (95% CI, 1.9-2.8 months).

The proportion of pts who achieved a CS dose of ≤7.5 mg/day at any time was higher with RUX vs BAT (71.5% [118/165] vs 61.6% [101/164]). This proportion was similar between RUX and BAT responders (69.8% [88/126] vs 71.7% [71/99]) and numerically lower in BAT vs RUX nonresponders (46.2% [30/65] vs 76.9% [30/39]). RUX also led to higher rates of CS discontinuation vs BAT overall (48.5% [80/165] vs 35.4% [58/164]), in responders (42.9% [54/126] vs 33.3% [33/99]), and nonresponders (66.7% [26/39] vs 38.5% [25/65]).

Image:

Figure. Median Percentage Change From BL in CS Dose by BOR



Patients, n												
RUX-Res	121	121	120	119	117	114	112	106	105	104	100	98
BAT-Res	97	97	97	96	93	92	92	89	87	85	84	81
RUX-NR	38	37	37	34	33	32	29	26	22	21	20	20
BAT-NR	56	55	51	50	49	46	45	45	43	38	36	35

BAT, best available therapy; BL, baseline; BOR, best overall response; CS, corticosteroid; NR, nonresponder; Res, responder; RUX, ruxolitinib.

Summary/Conclusion: RUX led to a faster and larger reduction in CS dose vs BAT, with a greater proportion of RUX-treated patients discontinuing CS treatment. Median decreases in CS dose were similar among RUX-treated pts, regardless of response. In contrast to RUX, BAT did not demonstrate a substantial CS-sparing effect in nonresponders. Further analyses assessing the impact of the CS-sparing effect observed with RUX are warranted.

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