Improvement in Serum Albumin as a Measure of Improved Metabolic Profile in Pacritinib-Treated Patients: A Retrospective Analysis of Patients Treated Across Three Clinical Trials

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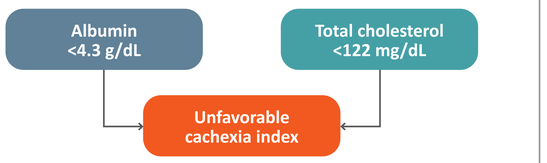
CONCLUSIONS

- Patients with myelofibrosis (MF) treated with pacritinib showed improvement in albumin
- Patients also maintained stable weight and normal cholesterol levels
- A correlation was observed between improvement in albumin and reduction in spleen volume
- A subset of patients were able to discontinue metformin after initiating treatment with pacritinib
- Further analysis from prospective studies is warranted to confirm these findings and assess other treatment-related metabolic effects

INTRODUCTION

- As an acute phase reactant and a marker of nutritional status, serum albumin is a prognostic marker in patients with MF, with levels tending to decrease over time
- An unfavorable cachexia index (**Figure 1**), based on albumin and cholesterol, is associated with inferior survival in patients with MF[1]

Figure 1. Cachexia index[1]



- Retrospective data in patients with MF suggest that the JAK1/2 inhibitor ruxolitinib is associated with increases in albumin, body weight and cholesterol[2,3]
- However, ruxolitinib is also associated with weight gain in many patients,[3] which may be perceived as bothersome by those without cachexia or even impact cardiovascular risk
- The metabolic profile of the JAK2/IRAK1/ACVR1 inhibitor pacritinib has not previously been described

AIM

- To investigate the metabolic profile of pacritinib and evaluate any correlation in serum albumin improvement and MF response outcomes

METHODS

- Patients with MF who were treated with pacritinib (200 mg twice daily or 400 mg once daily) in prior phase 3 clinical trials (PERSIST-1 [NCT01773187], PERSIST-2 [NCT02055781]), and the phase 2 PAC203 (NCT04884191) trial were included in this analysis
- Shifts in albumin, weight, and cholesterol were analyzed among patients with available week 12 or 24 data
- The linear correlation of changes in albumin and efficacy endpoints was measured via the Pearson correlation coefficient
- Data was summarized via data graphics such as boxplots, spaghetti, bar and line series plots
- Among patients requiring treatment for diabetes, changes in medication dosing were analyzed

REFERENCES: **1.** Tefferi A, et al. *Blood Adv* 2018;2:1980–1984; **2.** Kuykendall AT, et al. *JCO Precis Oncol* 2024;8:e2300593; **3.** Mesa RA, et al. *Clin Lymphoma Myeloma Leuk* 2014;15:214–221.e1.

RESULTS

- In total, 484 patients treated with pacritinib were included in the pooled analysis; baseline characteristics are within **Table 1**
- At baseline, the vast majority of patients (93%) had normal or high body mass index (BMI; only about 2% of patients had BMI <18 kg/m^2)

Table 1. Baseline characteristics

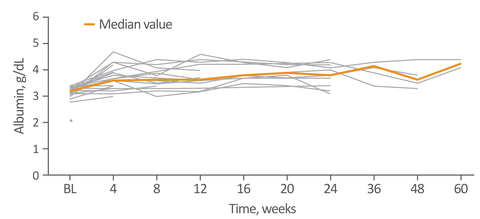
	Pacritinib N=484
Age (years), median (IQR)	68 (61, 73)
Male, n (%)	272 (56.2)
Race (White), n (%)	420 (86.8)
Weight (kg), median (IQR)	71.0 (60.9, 80.0)
BMI (kg/m^2), median (IQR)	24.5 (22.1, 26.9)
DIPSS high risk, n (%)	105 (21.7)
Platelet count (x10^9/L), median (IQR)	80 (41, 175)
Hemoglobin (g/dL), median (IQR)	9.8 (8.5, 11.4)
JAK inhibitor-naïve, n (%)	327 (67.6)
RBC transfusion-independent, n (%)	284 (58.7)

BMI, body mass index; DIPSS, Dynamic International Prognostic Scoring System; IQR, interquartile range; JAK, Janus kinase; RBC, red blood cell.

Albumin levels improve after initiating pacritinib

- In the subgroup of patients with baseline hypoalbuminemia (<3.5 g/dL), median albumin levels improved after initiation of pacritinib (**Figure 2**)

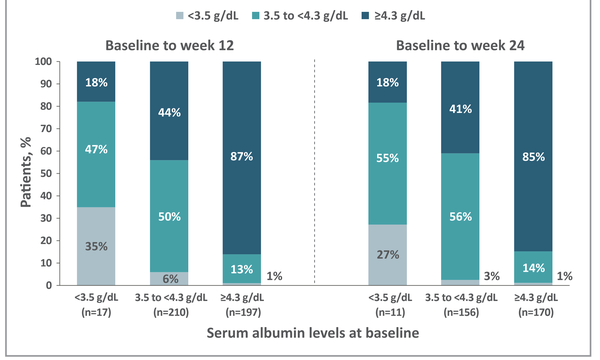
Figure 2. Serum albumin changes over time in patients with hypoalbuminemia at baseline



Albumin shift at week 12 and 24 with pacritinib

- Among patients with hypoalbuminemia (<3.5 g/dL) at baseline, 65% (11/17) had improvement to normal albumin levels at week 12, and 18% (3/17) had values ≥4.3 g/dL (**Figure 3**)
- Among patients with baseline albumin values ≥3.5 to <4.3 g/dL, 44% (93/210) improved to ≥4.3 g/dL, whereas only 6% (12/210) developed hypoalbuminemia (**Figure 3**)
- Among patients with higher baseline albumin values ≥4.3 g/dL, 87% (171/197) maintained values ≥4.3 g/dL (**Figure 3**)
- Similar trends were observed among patients at week 24, with 73% (8/11) of patients with baseline hypoalbuminemia improving to normal levels, 41% (64/156) with baseline intermediate values improving to values ≥4.3 g/dL, and 85% (144/170) with baseline albumin of ≥4.3 g/dL maintaining these levels (**Figure 3**)

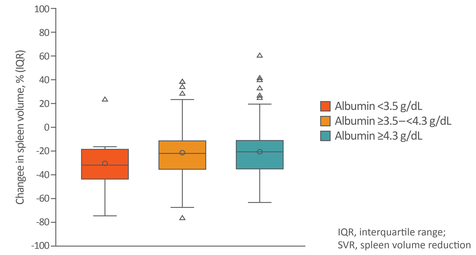
Figure 3. Shifts in albumin levels at week 12 and week 24



Pacritinib efficacy in patients with hypoalbuminemia

- Change in spleen volume was similar across baseline albumin groups, with no diminution in effect in patients with lower albumin levels (**Figure 4**)

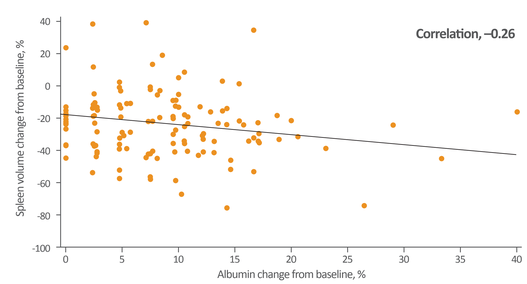
Figure 4. Change in spleen volume at week 24 by baseline albumin levels



Correlation between albumin improvement and spleen volume

- In patients with baseline albumin <4.3 g/dL, the correlation coefficient between improvement in albumin and reduction in spleen volume was –0.26 (**Figure 5**)

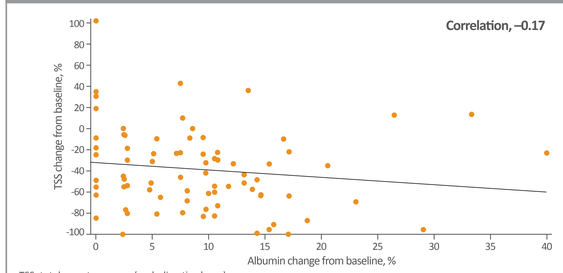
Figure 5. Spleen volume and albumin changes from baseline to week 24



Correlation between albumin improvement and total symptom score

- In patients with baseline albumin <4.3 g/dL, the correlation coefficient between improvement in albumin and reduction in symptom score was –0.17 (**Figure 6**)

Figure 6. TSS and albumin changes from baseline to week 24

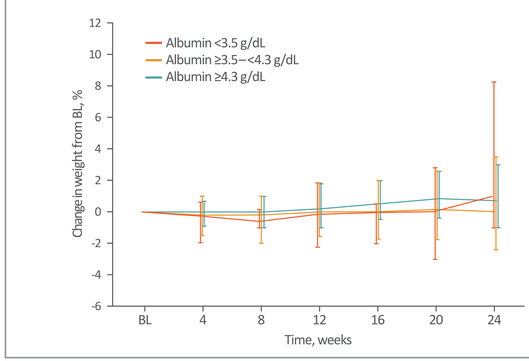


TSS, total symptom score (excluding tiredness)

Weight remains stable with pacritinib

- Regardless of baseline albumin level, weight remained stable in patients treated with pacritinib (**Figure 7**)

Figure 7. Percent change in weight over time by baseline albumin levels



Cholesterol remains stable with pacritinib

- Among patients with baseline total cholesterol levels less than 125 mg/dL, 24% (38/157) experienced an increase to ≥125 mg/dL, and none had an increase over 200 mg/dL at week 24

Effects of pacritinib on patients with diabetes

- Among 26 patients requiring metformin at study start, 19% (n=5) discontinued metformin while on treatment with pacritinib
- Among 15 patients requiring insulin at study start, 1 discontinued insulin on study treatment

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