THU0571 PRELIMINARY RESPONSE TO JANUS KINASE INHIBITION WITH BARICITINIB IN CHRONIC ATYPICAL NEUTROPHILIC DERMATOSIS WITH LIPODYSTROPHY AND ELEVATED TEMPERATURES (CANDLE)

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Background: Elevated serum IP-10 (CXCL10) levels and gene expression studies showing a prominent "interferon (IFN) signature" suggested modulation of IFN signaling might be a therapeutic option in CANDLE patients.
Objectives: The objective of this compassionate use program is to provide baricitinib (JAK1/JAK2 inhibitor) to CANDLE patients who have no other comparable or satisfactory treatment options. Potential efficacy of treatment was assessed by a reduction in mean Autoinflammatory Diary Scores (ADS) to <0.5 and reduction of steroid doses by at least 50% in patients receiving steroids at baseline.
Methods: Paired t-test was used to compare mean ADS and prednisone doses at the last NIH clinic visit to baseline data.
Results: Between October 2011 and January 1st, 2016, 11 CANDLE patients have been treated (mean duration 2.5 years (SD±1)). 9 of 11 patients achieved an ADS of <0.5 at the time of their last visit (mean ADS decreased from 1.3 ± 0.8 at baseline to 0.2 ± 0.3) ($p<0.005$), 8 of 10 patients achieved a reduction in steroids doses $>$ than 50% from baseline (mean total prednisone dose decreased from 0.8 mg/kg/day (0.2–1.8) to 0.2 mg/kg/day (0–1.1)) ($p<0.005$), 4 patients discontinued prednisone completely. The mean dose of baricitinib at the last patient visit was 6.9 ± 2.8 mg/day. 7 patients reported at least 1 serious adverse event (SAE), infection being the most common. 2 patients have been discontinued due to SAEs (avascular necrosis; BK viremia and azotemia). 1 patient required temporary interruption of baricitinib due to neutropenia, and 3 other patients had their dose electively reduced after testing positive for BK viremia: patients were asymptomatic. The most common adverse events were upper respiratory infections, cough, and BK viruria (baseline BK virus screening was not performed).1 patient died due to worsening interstitial lung disease with development of respiratory failure 4 months after discontinuation of baricitinib and initiation of another JAK inhibitor.
Conclusions: Preliminary efficacy data in 11 CANDLE patients treated with baricitinib are encouraging and suggest that targeting IFN signaling with a JAK1/JAK2 inhibitor may be a successful therapeutic strategy. Monitoring BK viral titers in blood and urine, in addition to other measures of safety and efficacy, may be important in dose selection and the benefit-risk assessment of baricitinib for CANDLE patients.
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