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POSTER ABSTRACTS

615.ACUTE MYELOID LEUKEMIAS: COMMERCIALLY AVAILABLE THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Improved Prevention and Treatment Strategy of Differentiation Syndrome Contribute to Reduce Early Death of Patients with Acute Promyelocytic Leukemia

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Purpose:
All-trans retinoic acid (ATRA) with arsenic trioxide (ATO) has been the standard of care for acute promyelocytic leukemia (APL) with high efficacy in china.However,early death (ED) still remains the major reason for treatment failure.Severe differentiation syndrome (DS) with no response to full dose dexamethasone is one of direct or indirect important causes of ED.Therefore,to further optimize prevention and treatment strategy of DS is critical for APL therapy success.
Patients and Methods:
The APL-01 study was a prospective and single-arm clinical trial in patients with newly diagnosed APL from June 2019 to December 2021.111 eligible patients aged between 18 and 70 years classified as Low-risk APL (WBC count at diagnosis$<10*10^9$/L n=78) or High-risk APL (WBC count at diagnosis$\geq 10*10^9$/L n=33) received induction therapy consisted of ATRA and intravenous arsenic trioxide or oral tetra-sulfide arsenic formulation (Realgar-Indigo naturalis formula,RIF) with chemotherapy-free or chemotherapy-substantially reduced protocol in China.
During the course of induction therapy,we used different intravenous doses of dexamethasone to prevent DS according to the WBC count at presentation or after the initiation of ATRA.For example,if WBC counts$\geq 5*10^9$/l and $<10*10^9$/l,5mg per day;if $\geq 10*10^9$/l,10mg per day.And we gave patients dexamethasone 10mg per 12h as preemptive therapy once DS was suspected.Ruxolitinib was administered when steroids therapy were considerd insensitive.

We evaluated the effect of selective steroids prophylaxis and preemptive therapy on the incidence and severity of DS,which contributed to increased early mortality rate. The safety and feasibility of Ruxolitinib as second-line therapy for DS was also explored.
Results:
In this study,41 of 111 patients (36.9%) experienced DS,16 (14.4%) were severe cases and 25 (22.5%) were moderate cases.
Univariate analysis identified the following prognostic factors as regards developing DS(P-value<0.1):age,sex and WBC count were included for exploring the difference between DS and Non-DS patients Increased WBC count (>4*10*109/l)(OR (95% CI)=1.241 (1.131-1.361)) were potential risk factors for patients with DS.We further investigated the difference between severe DS and moderate DS using age,sex,ECOG,WBC and PLT count.We found that only advanced age (over 40 years old)(OR (95% CI)=12.200 (1.640-90.772)) was associated with developing severe DS.
Dyspnea (71%),weight gain (85%) and pulmonary infiltrates(78%) were the most common symptoms of patients with DS.Compared with moderate DS,severe DS patients had more frequency of dyspnea (Fishers exact P=0.013),pleuropericardial effusion (χ2=5.577, P=0.018)and acute renal dysfunction (Fishers exact P=0.018).
Among the 41 patients with DS,23 patients were treated effectively with dexamethasone 10mg per 12h.18 patients with steroid resistance received Ruxolitinib to control the cytokine release storm(CRS),12 of which showed immediate remission, however,the situations of the remaining 6 patients did not alleviate until ATRA was suspended temporarily.All of them(6/41)recovered with the help of noninvasive mechanical ventilation.
The total 30-day mortality rate was 1.8% (2/111).During induction treatment,no death owing to DS or infection occurred.Two patients with high-risk APL died due to intracranial hemorrhage,one occurred on day 8 and the other on day 9 after ATRA were initiated.
Of all the 109 patients evaluable,78 (100%)Low-risk patients and 31 (100%) high-risk patients achieved complete remission (CR)at the end of induction therapy,respectively.The median follow-up time was 34 months,estimated 2-year overall survival (OS) was 98.7% in the Low-risk group and was 93.9% in the High risk group.
Conclusions:
Our study suggests individualized steroids prevention,preemptive treatment and Ruxolitinib as second-line therapy for DS contribute to control DS,which in verse lessen the discontinuation of ATRA, consequently decreasing early death due to DS and hemorrhage in APL patients.(clinicaltrials.gov NCT04446806)
Keywords:
acute promyelocytic leukemia;early death;prophylaxis strategy;pulmonary hemorrhage;differentiation syndrome;retinoid acid syndrome;Ruxolitinib;steroid-resistance;cytokine release syndrome;

Disclosures No relevant conflicts of interest to declare.

OffLabel Disclosure: We used Ruxolitinib as second-line therapy of differentiation syndrome to control the cytokine release syndrome.

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