COMBINED TREATMENT WITH SORAFENIB AND 5-AZACYTIDINE FOR NOT INTENSIVE CHEMOTHERAPY CANDIDATES PATIENTS WITH FLT3 MUTATED ACUTE MYELOID LEUKEMIA

Solé-Rodríguez M; Zapata Bautista R; Velarde López de Ayala P; Ramírez García S; Gil Espárraga E

Hospital Juan Ramón Jiménez, Huelva, Spain

INTRODUCTION

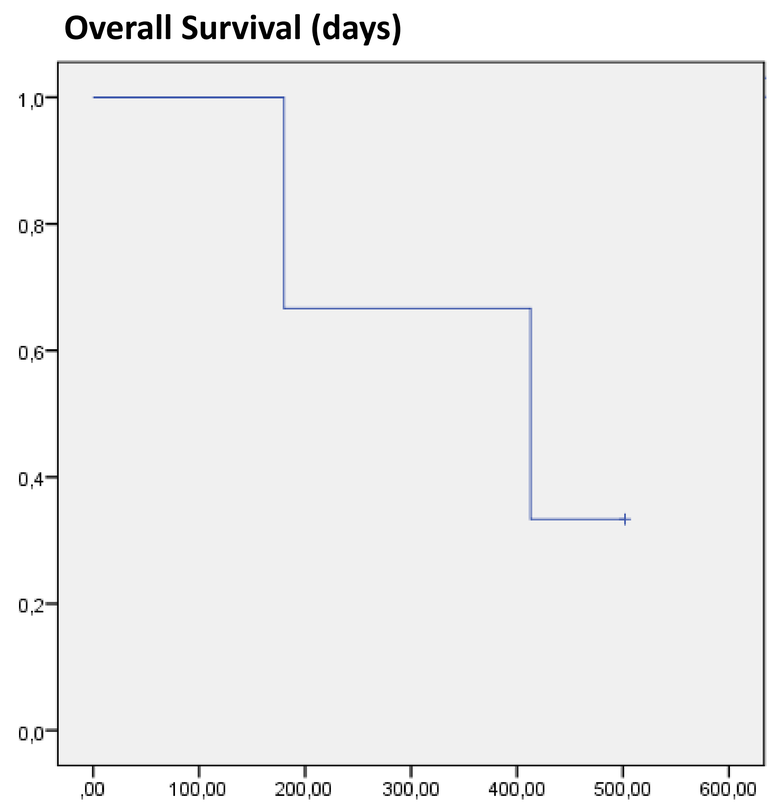
FLT3 mutations are one of the most common findings in acute myeloid leukemia (AML). Midostaurin is the first FLT3 inhibitor approved for FLT3 mutated AML (FLT3-AML) treatment in first line combined with intensive chemotherapy. However, there are not any FLT3 inhibitors currently approved for not intensive chemotherapy candidates FLT3-AML patients (unfit or refractory/relapse (R/R) patients). Combination of Sorafenib plus 5-azacytidine has showed promising results in this setting, so we use this combination when there is no clinical trial available.

Methods: We retrospectively evaluate the complications and outcome of FLT3-AML patients treated with this combination from January 2017 to August 2020.

RESULTS

Three patients were treated, all of them with FLT3-ITD mutation: one elderly patient as upfront therapy, one young patient due to refractory disease after two lines of intensive chemotherapy and the last one after early post-transplantation relapse. Patients have received a media of 12.6 courses of the combination (range 4-29). No patient discontinued treatment due to toxicity, including a patient treated concomitantly with Voriconazole for 5 months. Sorafenib dosage adjustment was required only in one patient due to diarrhoea. The patient who received the combination as upfront therapy is currently alive in complete response after 29 courses. The other two patients relapsed and dead after 8 and 14 months respectively. Progression free survival and overall survival (OS) for the entire group were 8,5 (range 3,6-16,7) and 12 (range 6-16,7) months respectively.

Baseline characteristics of patients and Outcome	
N	3
Age, years (median, range)	65,7 (61-74)
Gender, Male (frequency, percent)	1/3 (33 %)
Frontline therapy: ➢ 5-azacytidine plus Sorafenib ➢ Intensive Chemotherapy	1/3 (33%) 2/3 (66%)
Courses of 5-azacytidine plus Sorafenib (median, range)	12,6 (4-29)
Response to 5-azacytidine plus Sorafenib: ➢ Progressive disease (frequency, percent) ➢ Complete response (frequency, percent)	2/3 (66%) 1/3 (33%)
Complications attributable to treatment: ➢ Diarrhoea ➢ None	1/3 (33%) 2/3 (66%)



CONCLUSIONS

In our experience, Sorafenib combined with 5-aza is well tolerated and provides an acceptable OS in this particularly poor prognosis group. More studies are needed to define the role of this and other FLT3 inhibitors combinations in the future.

REFERENCES

Ohanian M, Garcia-Manero G, Levis M, Jabbour E, Daver N, Borthakur G, Kadia T, Pierce S, Burger J, Richie MA, Patel K, Andreeff M, Estrov Z, Cortes J, Kantarjian H, Ravandi F. Sorafenib Combined with 5-azacytidine in Older Patients with Untreated FLT3-ITD Mutated Acute Myeloid Leukemia. Am J Hematol. 2018 Sep;93(9):1136-1141. doi: 10.1002/ajh.25198. Epub 2018 Aug 31. PMID: 30028037.

Ravandi F, Alattar ML, Grunwald MR, Rudek MA, Rajkhowa T, Richie MA, Pierce S, Daver N, Garcia-Manero G, Faderl S, Nazha A, Konopleva M, Borthakur G, Burger J, Kadia T, Dellasala S, Andreeff M, Cortes J, Kantarjian H, Levis M. Phase 2 study of azacytidine plus sorafenib in patients with acute myeloid leukemia and FLT-3 internal tandem duplication mutation. Blood. 2013 Jun 6;121(23):4655-62. doi: 10.1182/blood-2013-01-480228. Epub 2013 Apr 23. PMID: 23613521; PMCID: PMC3674666.

Campregher PV, Mattos VRP, Salvino MA, Santos FPS, Hamerschlak N. Successful treatment of post-transplant relapsed acute myeloid leukemia with FLT3 internal tandem duplication using the combination of induction chemotherapy, donor lymphocyte infusion, sorafenib and azacitidine. Report of three cases. Einstein (Sao Paulo). 2017 Jul-Sep;15(3):355-358. doi: 10.1590/S1679-45082017RC3784. Epub 2017 Jul 24. PMID: 28746590; PMCID: PMC5823052.

Sid S, Rey J, Charbonnier A, D'Incan E, Mohty B, Blaise D, Vey N. Treatment of Post-transplant Relapse of FLT3-ITD Mutated AML Using 5-Azacytidine and Sorafenib Bitherapy. Clin Lymphoma Myeloma Leuk. 2017 Apr;17(4):241-242. doi: 10.1016/j.clml.2016.10.002. Epub 2017 Jan 11. PMID: 28196687.

CONTACT

Solé-Rodríguez M, masrodriguez5983@gmail.com