Exposure toxicity of venetoclax in acute myeloid leukemia patients in the real-life setting: impact of high exposure on delayed neutropenia

Authors

Florent Puisset,[1,2,3] Emmanuel Raffoux,[4] Lionel Ades,[5] Tony Huynh,[5] Raphaël Itzykson,[4] Didier Bouscary,[6] Loréa Aguinaga,[5] Florence Rabian,[4] Marie Sebert,[5] Anne Vekhoff,[7] Eolia Brissot,[7] Mohamad Mohty,[7] Agnes Bonnin,[7] Alexis Genthon,[7] Jeremie Zerbit,[6,8] Lise Willems,[6] Justine Decroocq,[6] Adrien Contejean,[6] Etienne Lengline,[4] Samia Mourah[1,9] and Lauriane Goldwirt[1,9]

[1]AP-HP, Hôpital Saint-Louis, Department of Pharmacology, Paris; [2]Centre de Recherches en Cancérologie de Toulouse (CRCT), Team 14, INSERM UMR1037, Université de Toulouse, Toulouse; [3]Pharmacy Department IUCT (Institut Universitaire du Cancer) Oncopole, Institut Claudius Regaud, Toulouse; [4]AP-HP, Hôpital Saint-Louis, Department of Hematology, INSERM U944, Paris; [5]AP-HP, Hôpital Saint-Louis, Department of Senior Hematology, INSERM U944, Paris; [6]AP-HP, Hôpital Cochin, Department of Hematology, Paris; [7]AP-HP, Hôpital Saint-Antoine, Department of Hematology, Paris; [8]AP-HP, Department of Pharmacy, Paris Public Hospital at Home, Paris and [9]INSERM U976, Université Paris Cité, Paris, France

Correspondence:
L. GOLDWIRT - lauriane.goldwirt@aphp.fr

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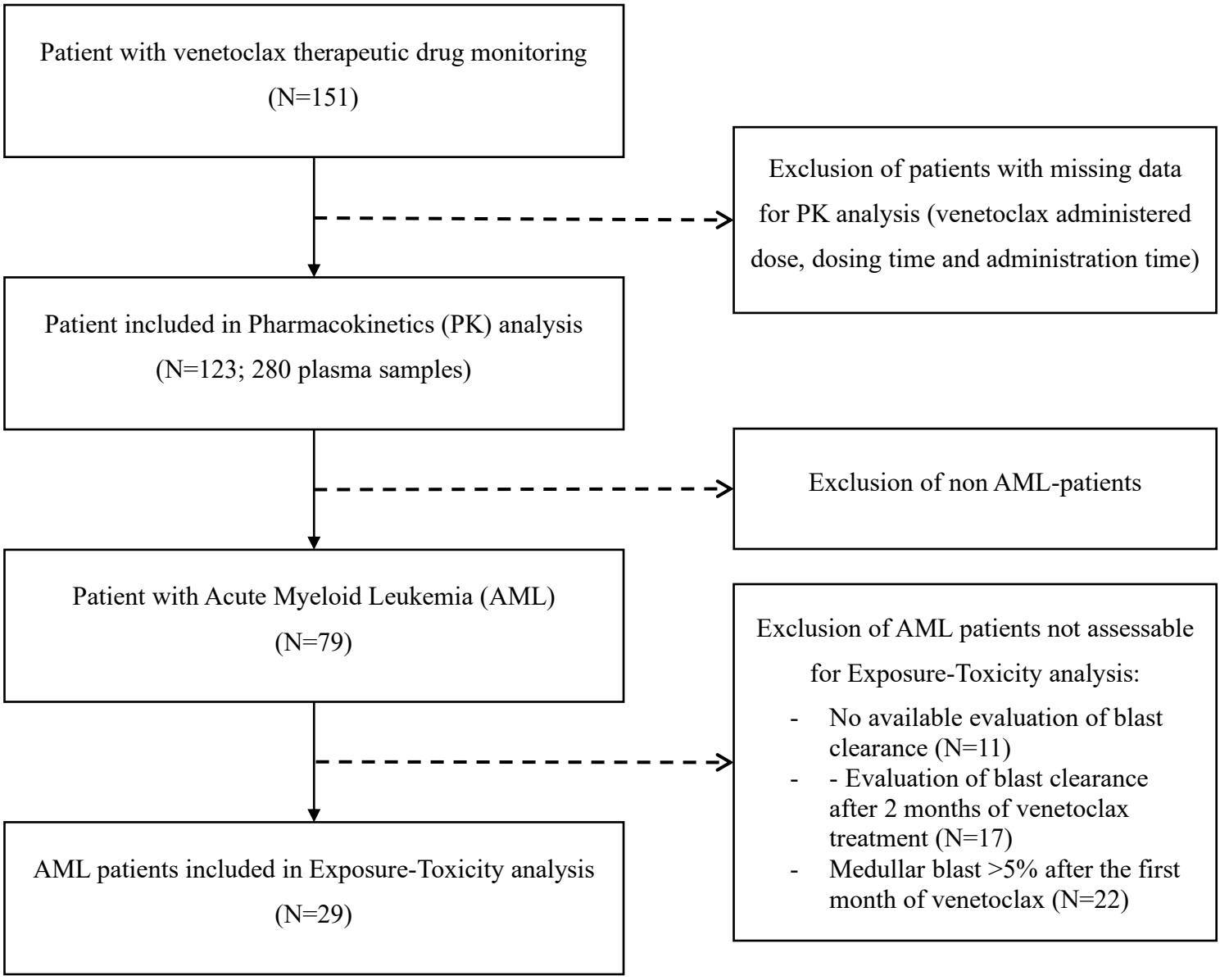
Supplemental data

Supplemental Figure 1. Flowchart patient inclusions in pharmacokinetic analysis and exposure-response analysis



Supplemental Table 1: Characteristics of patients with plasmatic venetoclax concentration available for the pharmacokinetic analysis.

Characteristic	N = 123
Age (years), median [IQR]	69 [59, 75]
Sex, N(%)	
Men	81 (65.9%)
Women	42 (34.1%)
Body weight (kg), median [IQR]	68 (57, 77)
Unknown	2
WHO performance status ≥2, N (%)	30 (27.0%)
Unknown	12
Pathology, N(%)	
Acute Lymphoblastic Leukemia	7 (5.7%)
Acute Myeloblastic Leukemia	77 (62.6%)
Chronic Lymphocytic Leukemia	11 (8.9%)
Lymphoplasmacytic Lymphoma	1 (0.8%)
Mulitple Myeloma	10 (8.1%)
Myelodysplastic Syndrome	10 (8.1%)
Myéloïd Sarcoma	1 (0.8%)
Non Hodgkin Lymphoma	6 (4.9%)
Regimen, N (%)	
Monotherapy	4 (3.3%)
V_CD20 inhibitor	15 (12.2%)
V_cytarabine	3 (2.4%)
V_daratumumab	2 (1.6%)
V_enasidenib	1 (0.8%)
V_hypomethylating agent	83 (67.5%)
V_ibrutinib	1 (0.8%)
V_ivosidenib	1 (0.8%)
V_jak inhibitor	1 (0.8%)
V_midostaurin	1 (0.8%)
V_nelarabine	2 (1.6%)
V_proteasome inhibitor	9 (7.3%)
ddi with strong CYPA inhibitor, N (%)	75 (61.0%)
ddi with strong CYPA inducer, N (%)	11 (8.9%)
ddi with ABC (P-gp or BCRP) inhibitor, N (%)	96 (78.0%)

Supplemental Table 2. Pharmacokinetics analysis: Estimated values of pharmacokinetic parameters of the population pharmacokinetic model

Parameters	Typical Value	Relative Standard error (%)
Ka -Day^{-1}	3.73	Fixed
CL/F -L/day	204	11
Vc/F -L	132	14
Effect of strong CYP3A inhibitor on CL	0.223	11
Effect of strong CYP3A inducer on CL	2.89	19
BSV Vc/F-%	85.9	15
BSV CL/F-%	76.4	9
IOV CL/F-%	30.2	16
Proportional residual error	19.26	19

BSV : between subject variability; IOV : intra-occasion variability.

Supplemental Figure 2. Pharmacokinetics analysis: Graphical validation of population pharmacokinetic model: correlation between observed and individual predicted concentrations (left panel, R^2=0.985) ; and individual relative prediction error according to individual predicted concentrations (right panel, R^2=0.044).