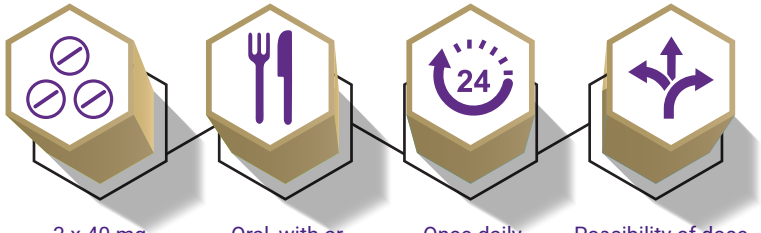

3 x 40 mg tablets[2] (Tablets shown are not of actual size)[1]

Oral, with or without food[1]

Once-daily monotherapy[1]

Possibility of dose adjustment, if needed[1]

FLT3: FMS-like tyrosine kinase 3, CRc: Composite complete remission, CRi: Complete remission with incomplete hematologic recovery, CRp: Complete Remission with partial haematologic recovery, HSCT: Haematopoietic stem cell transplant, AML: Acute Myeloid Leukaemia, LR: Late Responders, ER: Early Responders, OS: Overall Survival, E/PY: Events per Patient Year, TEAEs: Treatment Emergent Adverse Events CR: Complete Remission

References:
1. XOSPATA prescribing information (India-Version PI /India/Ver3.0/Jan 2023).
2. Perl AE, Martinelli G, Cortes JE, et al. Gliteritinib or chemotherapy for relapsed or refractory FLT3-mutated AML. N Engl J Med 2019; 381(18): 1728-1740.
3. Supplement to: Perl AE, Martinelli G, Cortes JE, et al. XOSPATA or chemotherapy for relapsed or refractory FLT3-mutated AML. N Engl J Med 2019;381:1728-40. DOI: 10.1056/NEJMoa1902688.
4. Perl AE, Larson RA, Podoltsev NA, et al. Follow-up of patients with R/R FLT3-mutation-positive AML treated with gilteritinib in the phase 3 ADMIRAL trial. Blood (Epub) 01-26-2022.
5. Ravandi F, Kantarjian H, Faderl S, et al. Outcome of patients with FLT3-mutated acute myeloid leukemia in rst relapse. Leukemia Res 2010;34(6):752-6.
6. Stone RM, DeAngelo DJ, Klimek V, et al. Patients with acute myeloid leukemia and an activating mutation in FLT3 respond to a small-molecule FLT3 tyrosine kinase inhibitor, PKC412. Blood. 2005;105(1):54–60. doi: 10.1182/blood-2004-03-0891
7. Fischer T, Stone RM, Deangelo DJ, et al. Phase IIB trial of oral Midostaurin (PKC412), the FMS-like tyrosine kinase 3 receptor (FLT3) and multi-targeted kinase inhibitor, in patients with acute myeloid leukemia and high-risk myelodysplastic syndrome with either wild-type or mutated FLT3. J Clin Oncol. 2010;28(28):4339–4345. doi: 10.1200/JCO.2010.28.9678

Additional information available on request

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Astellas Pharma India Private Limited
Unit No. 301, C & B Square, CTS Number 95 A, 127 Andheri Kurla Road,
Chakala, Andheri East, Mumbai, Maharashtra 400 069.
© 022 61557600 ◉ www.astellas.com ✉ pv@in.astellas.com

Scan for Xospata PI

XOSPATA gilteritinib

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STAY with XOSPATA™

A heartfelt thank you for helping us impact more than 100 patients and transforming care with Xospata

XOSPATA is the first and only oral monotheraphy to deliver superior overall survival compared with salvage chemotherapy in R/R FLT3m+AML[1*]

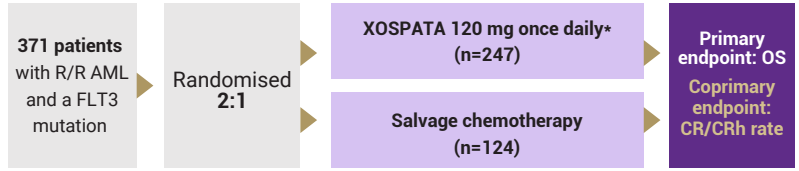
XOSPATA is the first drug that was approved and recommended as a targeted therapy for R/R FLT3 mutated AML[1]

1. In patients with AML, the presence of the FLT3 mutation adversely affects survival, both at diagnosis and on failure of the initial therapy[5]
2. For patients with R/R AML, other FLT3 inhibitors have not conferred durable clinical benefit as a single agent[6,7]
3. Xospata is a new, highly selective, oral FLT3 inhibitor with activity against both FLT3 mutation subtypes (ITD and TKD)[1]
4. To investigate the clinical benefit of Xospata in R/R FLT3-mutated AML, a multicenter, randomized trial was conducted[1]
5. XOSPATA monotherapy delivered unprecedented survival benefit with durable responses as compared to salvage chemotherapy[2]

XOSPATA monotherapy was evaluated in a phase 3 trial compared with Salvage Chemotherapy[2]

The ADMIRAL trial was a Phase 3, open-label, multicentre clinical trial that enrolled 371 adult patients with R/R FLT3m+ AML

ADMIRAL Study Design



Randomisation was stratified by patient response to 1L AML treatment and prespecified chemotherapy.† Prespecified chemotherapy regimens included:

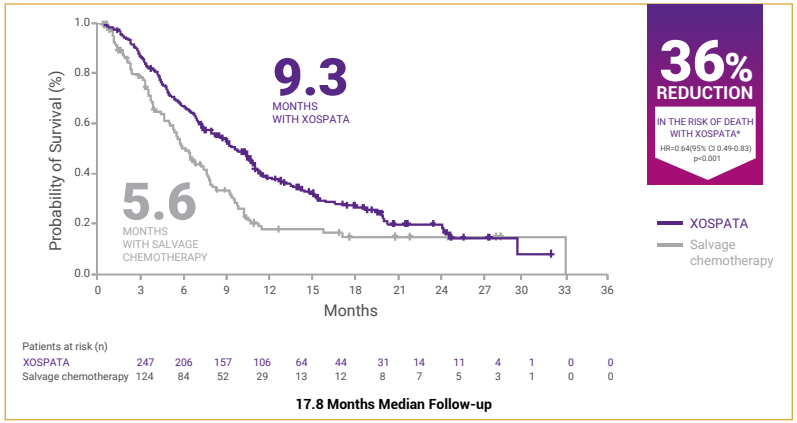
- High-intensity combination regimens MEC* and FLAG-IDA
- Low-intensity regimens LDAC11 and AZA¶

Baseline characteristics were well matched between the two groups[2]

Characteristic	All patients (N=371)	Gilteritinib (n=247)	Salvage chemotherapy (n=124)
Age, year			
Median	62.0	62.0	61.5
Range	19.0-85.0	20.0-84.0	19.0-85.0
Sex, n (%)			
Female	201 (54.2)	131 (53.0)	70 (56.5)
Cytogenetic risk status, n (%)			
Favourable	5 (1.3)	4 (1.6)	1 (0.8)
Intermediate	271 (73.0)	182 (73.7)	89 (71.8)
Unfavourable	37 (10.0)	26 (10.5)	11 (8.9)
Unknown	58 (15.6)	35 (14.2)	23 (18.5)
Previous therapy for AML, n (%)			
Anthracycline	311 (83.8)	205 (83.0)	106 (85.5)
FLT3 inhibitor	49 (13.2)	34 (13.8)	15 (12.1)
HSCT	74 (19.9)	48 (19.4)	26 (21.0)
Response to first-line therapy before enrolment, n (%)‡			
Relapse	**225 (60.6)**	**149 (60.3)**	**76 (61.3)**
Primary refractory AML without HSCT	**146 (39.4)**	**98 (39.7)**	**48 (38.7)**
Preselected salvage chemotherapy per IRT, n (%)			
High-intensity chemotherapy	**224 (60.4)**	**149 (60.3)**	**75 (60.5)**
Low-intensity chemotherapy	**147 (39.6)**	**98 (39.7)**	**49 (39.5)**
FLT3 mutation subtype, n (%)§			
ITD only	328 (88.4)	215 (87.0)	113 (91.1)
TKD only	31 (8.4)	21 (8.5)	10 (8.1)
ITD and TKD	7 (1.9)	7 (2.8)	0

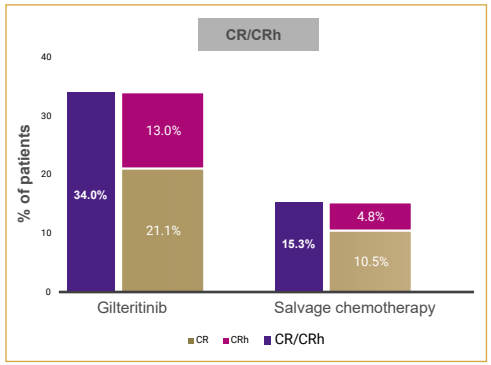
XOSPATA resulted in Significantly Longer Overall Survival than Salvage Chemotherapy in the Admiral Trial[2]

- New, highly selective, oral FLT3 inhibitor with activity against both FLT3 mutation subtypes (ITD and TKD)[1]



17.8 Months Median Follow-up

XOSPATA resulted in higher percentage of complete remission with full or partial hematologic recovery (CR/CRh) compared with salvage chemotherapy[2]



The percentage of patients who had complete remission with CR/CRh was 34.0% in the gilteritinib group vs 15.3% in the chemotherapy group

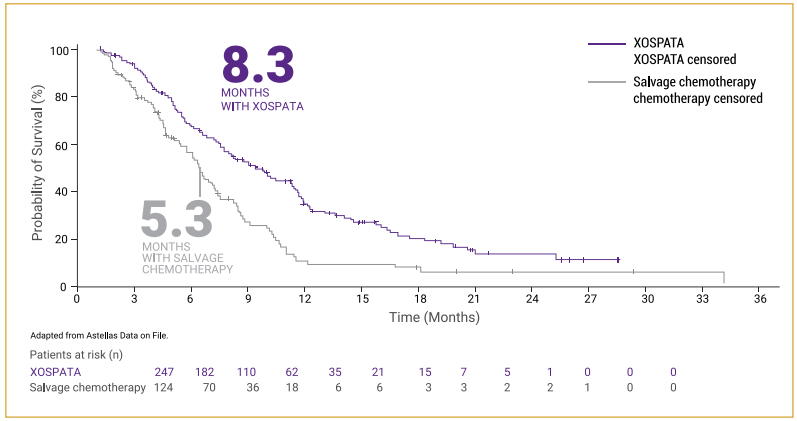
Risk difference: 18.6 percentage points (95% CI, 9.8 to 27.4)

The percentages of patients with CR were 21.1% in the gilteritinib group vs 10.5% in the chemotherapy group

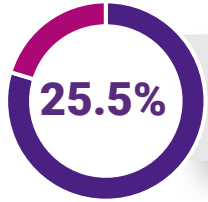
Risk difference: 10.6 percentage points (95% CI, 2.8 to 18.4)

Median Overall Survival advantage was maintained with XOSPATA, after censoring at the time of transplantation.[2]

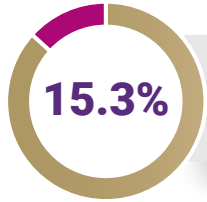
The OS advantage with XOSPATA was maintained after HSCT censoring



More patients proceeded to transplant receiving XOSPATA treatment versus salvage chemotherapy[2]



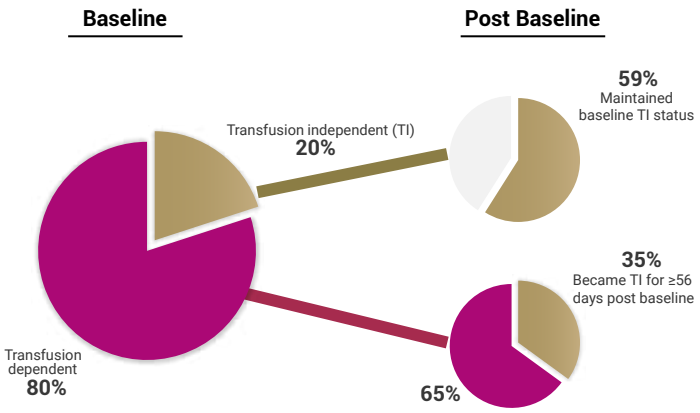
of patients in the gilteritinib arm went on to receive a transplant (63/247)



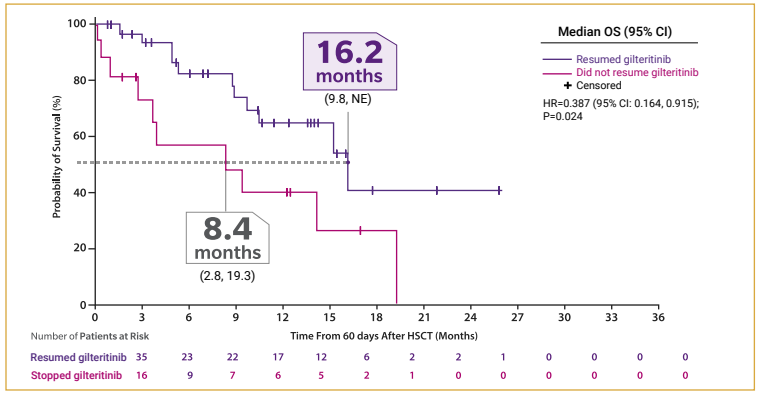
of patients proceeded to transplant in the SC group (19/124)

Transfusion Independence was achieved by 35% of patients and maintained by 59% of patients with XOSPATA[2]

Overall, 197 of 247 patients (79.8%) who had been randomly assigned to the Gilteritinib group were transfusion-dependent at randomization. A total of 68 of these 197 patients (34.5%) became transfusion-independent.



Prolonged survival was observed post-HSCT in the XOSPATA arm: effect of maintenance therapy (landmark analysis from day 60 post-HSCT; N=51)[2]



XOSPATA has a well-established long-term safety profile[2]

- Of the 247 patients, the most common serious adverse events that were considered to be related to Xospata therapy were febrile neutropenia (23 patients [9.3%]), ALT increase (n=11; 4.5%) and AST increase (n=10; 4.1%)
- Prolonged QTcF interval of any grade, possibly related to gilteritinib, occurred in 12 patients (4.9%), but only 1 patient (0.4%) had a maximum post baseline increase in the mean QTcF interval of more than 500 msec

TEAEs in ≥25% of Patients in Any Treatment Arm, n (%)				
	Gilteritinib (n=246)		Salvage Chemotherapy (n=109)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Anemia	116 (47)	100 (41)	38 (35)	33 (30)
Febrile neutropenia	115 (47)	113 (46)	40 (37)	40 (37)
Pyrexia	105 (43)	8 (3)	32 (29)	4 (4)
ALTincreased	103 (42)	34 (14)	10 (9)	5 (5)
AST increased	99 (40)	36 (15)	13 (12)	2 (2)
Nausea	79 (32)	5 (2)	36 (33)	0
Diarrhea	81 (33)	9 (4)	32 (29)	3 (3)
Constipation	76 (31)	2 (<1)	16 (15)	0
Cough	72 (29)	1 (<1)	11 (10)	0
Hypokalemia	71 (29)	32 (13)	34 (31)	12 (11)
Fatigue	70 (28)	6 (2)	14 (13)	2 (2)
Headache	64 (26)	3 (1)	16 (15)	0
Thrombocytopenia	63 (26)	56 (23)	18 (17)	18 (17)
Platelet count decreased	56 (23)	54 (22)	28 (26)	27 (25)

- **Incidence of exposure-adjusted grade ≥3 adverse events was 19.34/PY and 42.44/PY in the gilteritinib and chemotherapy arms, respectively**
- Mortality at 30 days: 2.0% in Gilteritinib group versus 10.2% in salvage chemotherapy group
- Mortality at 60 days: 7.7% in Gilteritinib group versus 19% in salvage chemotherapy group

Median duration of exposure to treatment was higher in XOSPATA group as compared to chemotherapy group[2]

- The median duration of exposure to XOSPATA was 18 weeks (interquartile range, 9 to 34), treatment exposure was 121.7 patient-years
- The median duration of exposure to chemotherapy was 04 weeks (interquartile range, 4 to 4), treatment exposure was 11.9 patient-years

Incidence of all exposure-adjusted adverse events Including those that were considered drug- related
HIGHER IN CHEMOTHERAPY GROUP

AEs occurred during the first 30 days of treatment, except for elevations of the liver amino transferase levels
HIGHER IN CHEMOTHERAPY GROUP

Efficacy benefit of XOSPATA in sub group of patients[2,3]

- Overall Survival and Response Rates According to Chemotherapy Intensity and Transplantation Status (Intention-to-Treat Population)

Parameter	Gilteritinib	Salvage Chemotherapy	
Median Overall Survival			**Hazard Ratio (95% CI)**
High-intensity chemotherapy	10.5 months	6.9 months	0.663 (0.471, 0.932)
Low-intensity chemotherapy	6.4 months	4.7 months	0.563 (0.378, 0.839)
Received prior HSCT	8.3 months	4.0 months	0.480 (0.274, 0.840)
Did not receive prior HSCT	9.6 months	6.0 months	0.684 (0.511, 0.917)
CR Rate, no. (%)			**Risk Difference (%) (95% CI)**
High-intensity chemotherapy	37/149 (24.8%)	12/75 (16.0)	8.8 (−3.0, 20.6)
Low-intensity chemotherapy	15/98 (15.3%)	1/49 (2.0)	13.3 (3.6, 22.9)
Received prior HSCT	17/48 (35.4%)	3/26 (11.5)	23.9 (2.6, 45.1)
Did not receive prior HSCT	35/199 (17.6%)	10/98 (10.2)	7.4 (−1.4, 16.1)
Before on-study HSCT	34/247 (13.8%)	13/124 (10.5)	3.3 (−4.0, 10.5)
CR/CRh Rate, no. (%)			**Risk Difference (%) (95% CI)**
Before on-study HSCT	65/247 (26.3%)	19/124 (15.3)	10.9 (2.4, 19.5)

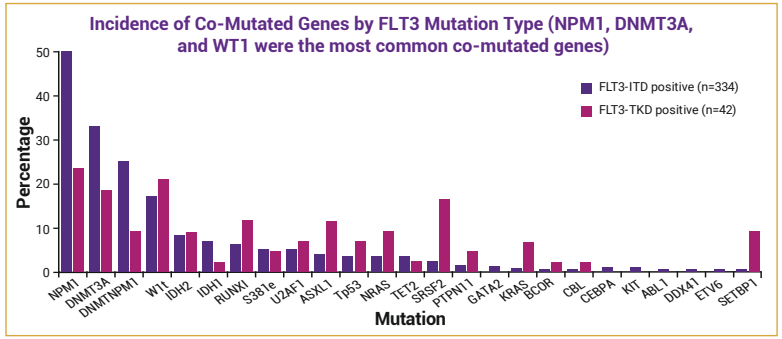
Response seen in patients treated with XOSPATA after dose adjustment (intention-to-treat population)[2,3]

Remission Parameter	Gilteritinib Dose Increased to 200 mg (n=78)	Gilteritinib Dose Decreased to 80 mg (n=58)
CR, no. (%)	7 (9.0)	14 (24.1)
Crh, no. (%)	5 (6.4)	10 (17.2)
CR/CRh, no. (%)	12 (15.4)	24 (41.4)
Crc, no. (%)	25 (32.1)	32 (55.2)

Overall survival and complete remission rates by FLT3 mutation type was higher in Xospata arm as compared to salvage chemotherapy (ITT*)[2,3]

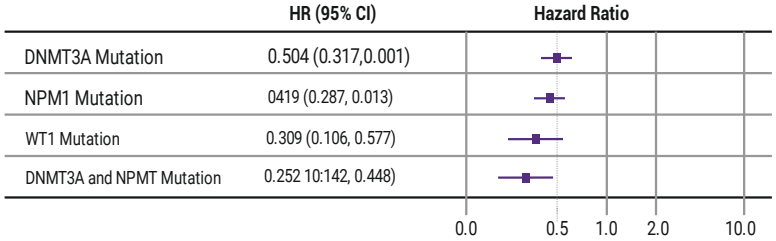
Response Parameter	FLT3-ITD alone*			FLT3-TKD Alone*		
	Gilteritinib (n=215)	Salvage Chemotherapy (n=113)		Gilteritinib (n=21)	Salvage Chemotherapy (n=10)	
Median OS, months			HR (95% CI)			HR (95% CI)
	9.3	5.6	0.623 (0.473, 0.820)	8.0	5.7	0.693 (0.293, 1.643)
CR, no. (%)			Risk difference (%) (95% CI)			Risk difference (%) (95% CI)
	44 (20.5)	11 (9.7)	10.7 (2.4, 19.1)	4 (19.0)	2 (20.0)	−1.0 (−38.3, 36.4)

Efficacy benefit of XOSPATA in sub group of patients[2,3]



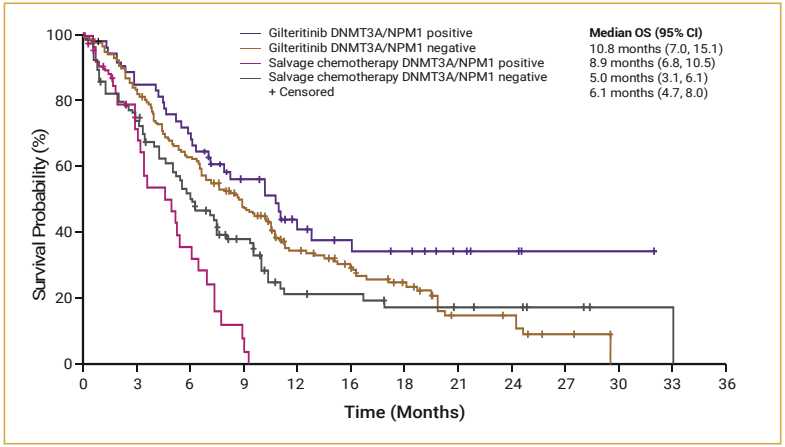
Survival benefit with XOSPATA is seen regardless of co-mutations[2,3]

Gilteritinib vs salvage chemotherapy for positive co-mutation status



AXL Flow Category	Gilteritinib 120 mg/day Ratio	Salvage Chemotherapy HR (95% CI)	Hazard
> Median Percent AXL Positive Blast at Baseline	88/120	43/54	0.608 (0.420, 0.879)
<Median Percent AXL Positive Blast at Baseline	79/122	36/51	0.709 (0.475, 1.056)

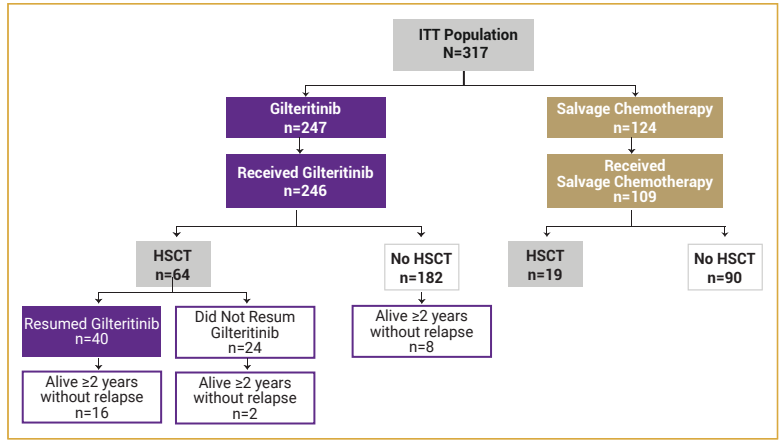
Patients with both NPM1 and DNMT3A co-mutations (23% in the XOSPATA arm) showed the greatest survival benefit from XOSPATA[2,3]



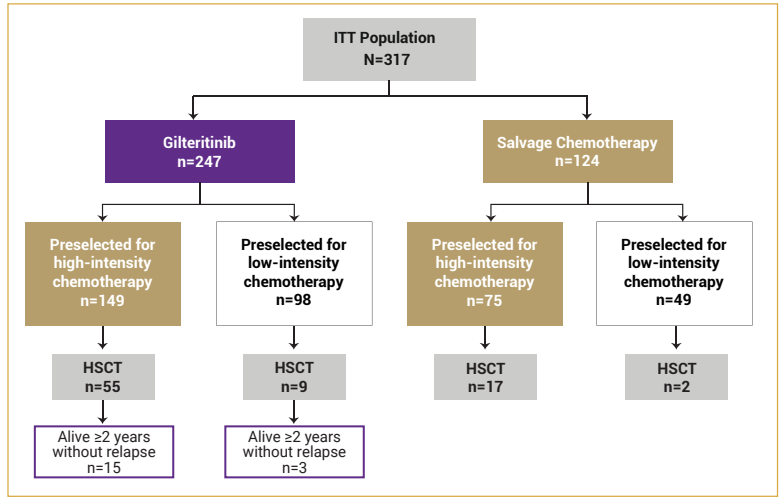
ADMIRAL TRIAL: 2 year long-term follow up data

Patient Disposition by Treatment Received[4]

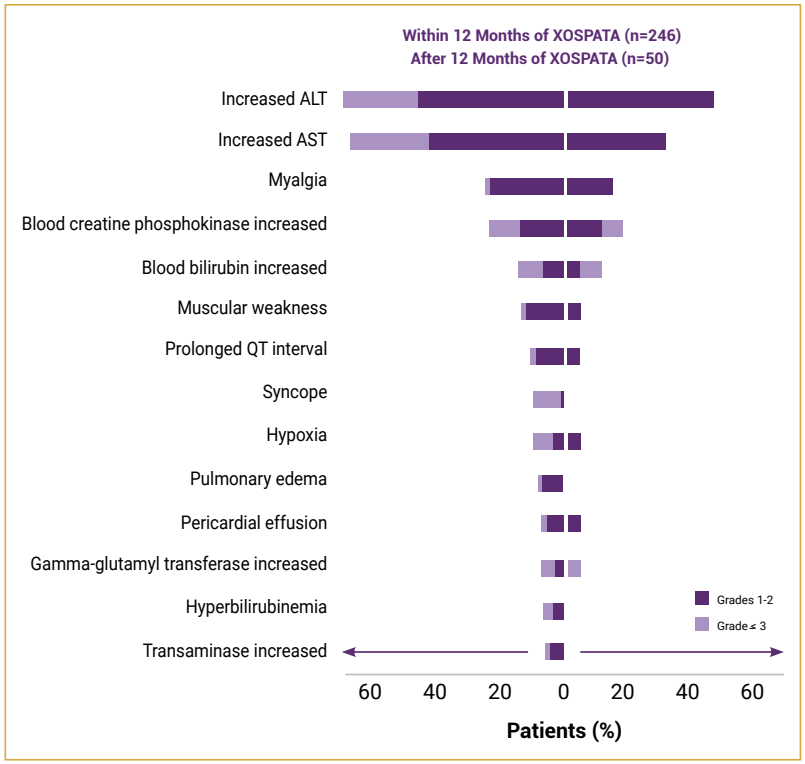
Data cutoff date: September 20, 2020 Median survival follow-up: 37.1 months



Patient disposition by Preselected Chemotherapy : Patients remain alive for ≥2 Years without relapse in the XOSPATA Arm[4]



Adverse Events of Interest During and After First Year of XOSPATA Therapy[4]



- The overall incidence of ARs declined during the second year of treatment (Year1:14.2% [n=35/246]; Year 2:8% [n=S/50])[28]

The safety profile of XOSPATA was stable over a 2-year period with no new or clinically significant safety signals[4]

Dose Modifications to Manage XOSPATA-Related Toxicities[1]

In the absence of response (patient did not achieve CRc) after 4 weeks of treatment, the dose can be increased to 200 mg (five 40 mg tablets) once daily, if tolerated or clinically warranted[1]

The daily dose can be reduced from 120 to 80 mg or from 200 to 120 mg[1]	
Symptoms of differentiation syndrome	If differentiation syndrome is suspected, administer corticosteroids and initiate haemodynamic monitoring. XOSPATA should be interrupted if severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids. Treatment with XOSPATA can be resumed at the same dose when signs and symptoms improve to Grade 2" or lower
Symptoms of posterior reversible encephalopathy syndrome[1]	XOSPATA should be discontinued.
QTcF Interval >500 msec[1]	XOSPATA should be interrupted. Resume XOSPATA at a reduced dose (80 or 120 mgt) when QTcF interval returns to within 30 msec of baseline or 5480 msec.
QTcF Interval Increased by >30 msec on electrocardiogram on Days of Cycle 1[1]	Confirm with electrocardiogram on Day 9. If confirmed, consider dose reductionto 80mg.
Symptoms of pancreatitis[1]	XOSPATA should be interrupted until pancreatitis is resolved. Treatment with XOSPATA can be resumed at a reduced dose (80 or 120 mg[1]).
Other Grade 3 or higher toxicity considered related to treatment[1]	XOSPATA should be interrupted until toxicity resolves or improves to Grade 1.* Treatment with XOSPATA can be resumed at a reduced dose (80 or 120 mg[1]).
Planned HSCT[1]	Interrupt treatment with XOSPATA 1 week prior to administration of the conditioning regimen for HSCT. Treatment can be resumed 30 days after HSCT if engraftment was successful, the patient did not have Grade >2 acute GVHD, and the patient was in CRc.[1]