BSH 2020 VIRTUAL
9 -14 NOVEMBER

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19 Courses of CPX-351 for the treatment of AML

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INTRODUCTION

CPX-351 is a liposomal encapsulated formulation of daunorubicin and cytarabine in a fixed 1:5 molar ratio. In phase 3 trials it has shown a survival benefit in high-risk or secondary AML [1, 2]. It has been approved by NICE for use within its marketing authorisation of "'the treatment of adults with newly diagnosed, therapy-related acute myeloid leukaemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC)" [3].

It has, however, been more widely used in a clinical trial context and the experience of its use within Belfast City Hospital for patients enrolled on the AML19 trial have been collated and analysed.

METHOD

1. Medical notes and laboratory records were reviewed for each course of CPX that commenced between 01/01/2017 and 31/05/2019 in Belfast City Hospital (19 courses involving 12 patients).
2. For each of these courses data was recorded on the time to platelet/neutrophil nadir, last red cell/platelet transfusion (as proxies for red cell and platelet recovery), neutrophil recovery (>0.5 x 109/L) and discharge. In addition total duration of antimicrobials was recorded as well as any adverse events that occurred prior to discharge.
3. For each patient involved data on previous chemotherapy as well as baseline statistics (including cytogenetics) were recorded.

RESULTS

These charts summarise the main findings in the review of count recovery time and antibiotic for all 19 courses of CPX-351 reviewed in our patient cohort.

Chart 1: A breakdown of antibiotic use by patient and course of CPX-351 (e.g. A-1 means patient A, course 1 of CPX-351).

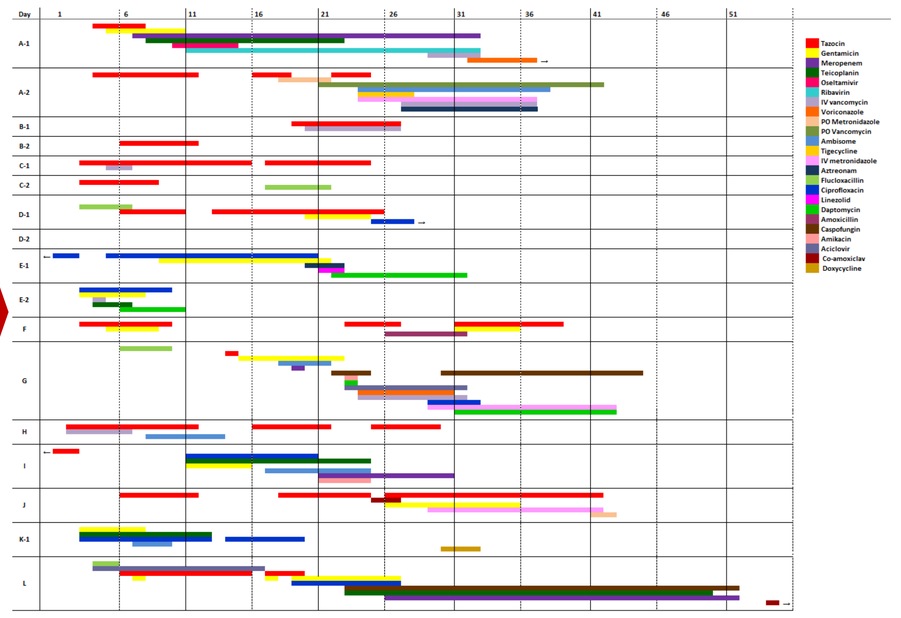
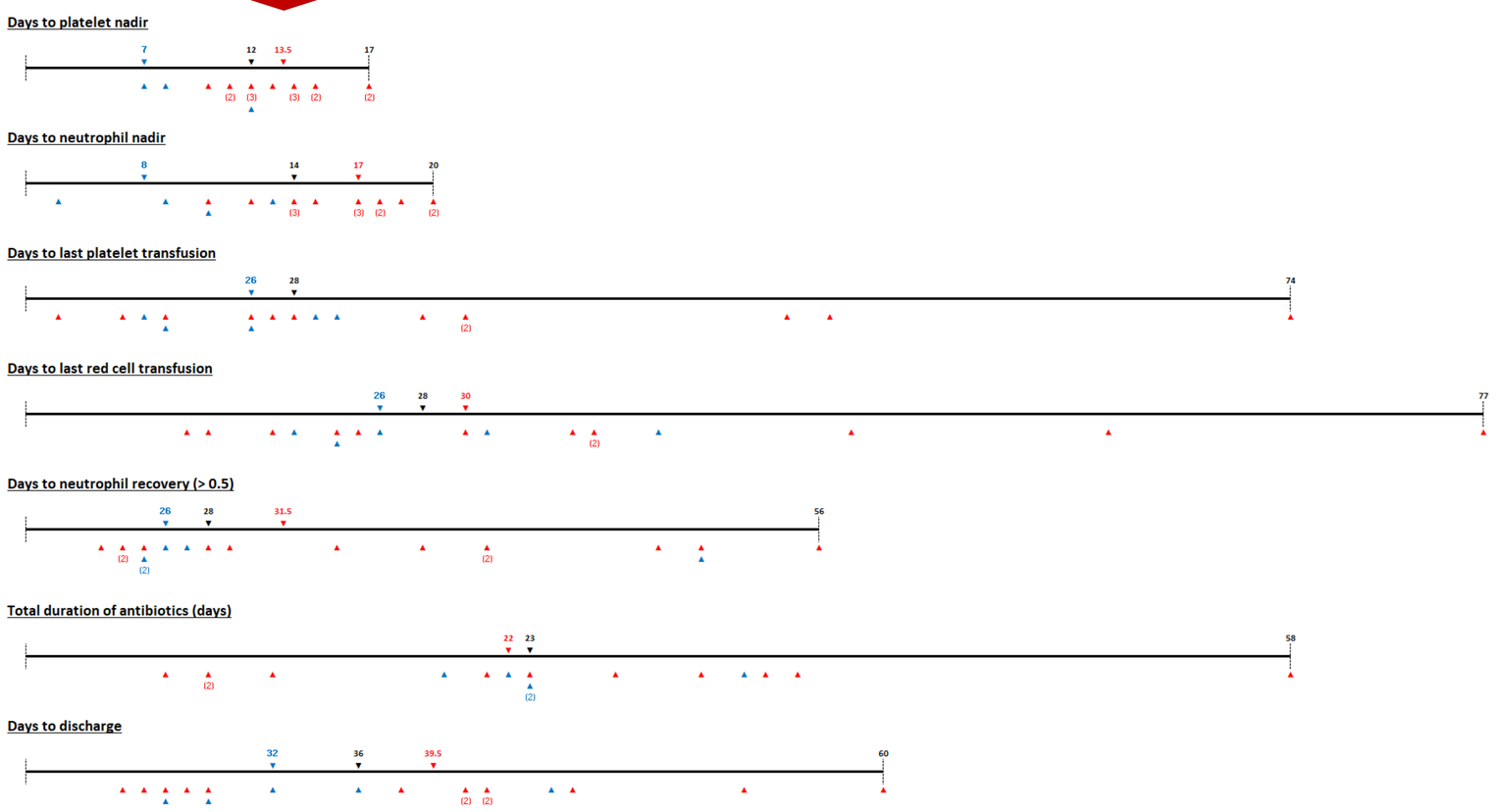


Chart 2: Overview of time to count nadir/recovery/discharge and antibiotic duration by course of CPX-351.

Indicators above the line represent median values, those below the line indicate individual patient. Blue = first course; Red = subsequent courses. Black = median value overall.



PATIENT CHARACTERISTICS

	Diagnosis	Date of Dx	Age at Dx	C1		C2		C3		Outcome	Transplant?	Relapse?	Next	Deceased?
				Regime	D1	Regime	D1	Regime	D1					
A	AML-MRC	12/01/2017	58	CPX	30/01/2017	CPX	28/03/2017	CPX	26/06/2017	Refractory	No	N/A	Aza	Feb 2018
B	AML	08/03/2017	46	FLAG-Ida+GO1	13/03/2017	CPX	15/05/2017	CPX	26/06/2017	Remission	23/08/2017	05/02/2019	Aza	No
C	AML	19/04/2018	53	FLAG-Ida+GO1	25/04/2018	CPX	11/06/2018	CPX	24/07/2018	Remission	01/10/2018	No	N/A	No
D	MDS-RAEB2	22/02/2017	53	CPX	06/03/2017	CPX	19/04/2017	FLAG-Ida	18/07/2017	Refractory AML	No	N/A	Aza	Dec 2017
E	AML	26/04/2017	39	DA3+10+GO2	12/05/2017	CPX	10/07/2017	CPX	20/09/2017	Remission	31/10/2017	No	N/A	No
F	AML	05/04/2017	36	DA3+10	12/04/2017	CPX	08/06/2017			Refractory	No	N/A	Supportive	Oct 2017
G	AML	05/04/2018	57	FLAG-Ida+GO2	18/04/2018	CPX	25/06/2018			Refractory	10/09/2018	13/11/2018	Supportive	Jan 2019
H	AML	12/04/2018	60	CPX	22/04/2019					Ongoing				No
I	AML	01/04/2019	41	CPX	08/04/2019					Ongoing				No
J	AML	20/02/2019	41	Flag-Ida	26/02/2019	CPX	10/04/2019			Ongoing				No
K*	Relapsed AML	05/03/2019	24	CPX	18/03/2019	CPX	27/05/2019			CNS relapse on treatment	Planned	13/09/2019	HD Ara-C	No
L	AML	22/02/2019	43	FLAG-Ida	27/02/2019	CPX	15/04/2019			Ongoing				No

*** Previously treated with FLAG-Ida+GO, FLAG-Ida & 2 x HD Ara-C between 28/03/2018 and 06/06/2018**

Patient	Karyotype	Patient	Karyotype
A	45,XX,add(3)(p21),-5[2]/45,idem,del(7)(p12p22),t(9;15)(q34;q15)[8]	G	Failed at diagnosis (subsequently 46,XY[30] post-treatment)
B	46,XY,del(7)(q11.2q36)[4]/46,XY[16]	H	43~45,XY,-3, inv(3)(p12q26), add(5)(q31), del(5)(q13q35), der(6)(5qter->5q31::6p2?3->6qter), -7, -13, ?14, -20, +4mar[cp9]/46, XY[1]
C	46,XY[20]	I	45, XX, del(5)(q31q35), der(6)(?::6p21->6q27::11q23->11q2?5::?), der(11)t(6;11)(q27;q23), der(12;17)(q10;q10)[6]/46, idem,+8[4]
D	45,XY,-7[12]/46,XY[1]	J	45,XY,t(3;21)(q26;q22),-7[10]
E	46,XY[20]	K	47,XX,i(7)(q10),+8[10]
F	46,XX[20]	L	46,XX[20]

DISCUSSION

In this sample, from day 1 of treatment the median time to platelet/neutrophil nadir, last platelet transfusion, last red cell transfusion and neutrophil recovery is recorded above. Prolonged time to count recovery has already been noted in previous clinical trials with CPX-351 with median time to neutrophil recovery reported at 35 days compared with 29 days for DA 7+3 [1]. This difference is not evident in our, much smaller sample, at with a median recovery of 28 days, although the range was quite wide at 20-56 days.

Excluding febrile neutropaenia, which was the most common adverse event, 32 other adverse events were noted across all courses of treatment. The most common was rash in 13 of 19 courses often similar to folliculitis in appearance.

Overall CPX-351 was well tolerated in the patient cohort reviewed. One aspect that was not frequently recorded in the medical notes but which was evident on discussion with patients is that hair loss is relatively uncommon with CPX-351 unlike with other intensive chemotherapy regimens.

REFERENCES

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