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Orbital extramedullary leukaemia is not a rare entity

I read with great interest the paper by Ohanian *et al* (2018), in which they reported the rarity of orbital extramedullary myeloid leukaemia (EML) and discussed the management of their 10 cases. However, orbital EML is not a rare entity–ocular chloroma was presented in 1970 at the 13th International Congress of Haematology (Cavdar *et al*, 1971). The same group reported ocular granulocytic sarcoma in 20 of 56 cases with acute myelomonocytic leukaemia (AMML) and designated them as chloroma-like deposits (granulocytic or myeloid sarcomas) in the eye and orbit (Cavdar *et al*, 1978a). These children showed a rapid response to anti-leukaemic therapy and the presence of antigen (type-C virus?) was identified in one patient (Cavdar *et al*, 1978a). In the same year Cavdar *et al* (1978b) presented ultrastructural findings of ocular granulocytic sarcoma in 12 cases, including intracytoplasmic structure resembling virus-like particles in three bone marrow samples and one eye sample. Cavdar *et al* (1989) reported 33 cases of Turkish children presenting with orbito-ocular granulocytic sarcoma (OOGS), characterized by exophthalmos, chemosis and orbital masses, and orbital tumours by light and electron microscope investigations with, despite similar haematological parameters, shorter mean survival times for patients with and without OOGS (8·7 months vs. 28·6 months). The authors concluded that these cases may be classified as a "high risk" subgroup of childhood AMML (Cavdar *et al*, 1989). The Cavdar group then studied the biology of OOGS and reported a higher incidence of EML in cases with M4 and M5 subtype, expression of P-glycoprotein, CD56 and CD44, and poor clinical outcome (Gözdaşoğlu *et al*, 2002). Several studies have emphasized the high incidence of OOGS (up to 60%) in male children with EML a t(8:21) from South African and Asian patients, despite the fact that this entity is unusual in the Western World, and proposed the possible role of race, sex, T-cell immunity and low socioeconomic status, together with more intensive chemotherapy regimens in these cases (Fleming, 1988; Schwyzer *et al*, 1998; Bisschop *et al*, 2001; Gözdaşoğlu *et al*, 2002).

In conclusion, orbital EML is not a rare entity; the biology and proposals for the management of this entity have been extensively studied by the Cavdar group. I am happy to share this data with other haemato-oncologists.

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Phase 1–2 safety, efficacy and pharmacokinetic study of decitabine in sequential administration with cytarabine in children with relapsed or refractory acute myeloid leukaemia

Epigenetic priming with DNA methyltransferase inhibitors may lead to better clinical outcomes when combined with induction chemotherapy. Preclinical data using primary paediatric acute myeloid leukaemia (AML) xenografts suggested that sequential dosing of decitabine and cytarabine might be more effective than either agent alone in refractory/relapsed paediatric AML (Leonard *et al*, 2014).

We conducted a phase 1–2 open-label, multicentre study to evaluate the safety, pharmacokinetics (PK) and clinical activity of decitabine in sequential administration with cytarabine in children with relapsed/refractory AML and to explore associated gene expression and DNA methylation profiles. The phase 1 primary objectives were to determine the maximum tolerated dose (MTD) of cytarabine that could be given on days 8–12 following decitabine 20 mg/m^2 on days 1–5 and to determine decitabine PK parameters. The phase 2 primary objective was to determine the response rate (complete remission

Table I. Adverse events in ≥10% of patients.

	Decitabine + Cytarabine (N = 17)				
Adverse events	Total	Grade 1	Grade 2	Grade 3	Grade 4
Anaemia	14 (82·4)	0	2 (11·8)	12 (70·6)	0
Thrombocytopenia	11 (64·7)	0	0	1 (5·9)	10 (58·8)
Febrile neutropenia	9 (52·9)	0	0	8 (47·1)	1 (5·9)
Pyrexia	9 (52·9)	1 (5·9)	5 (29·4)	3 (17·6)	0
Vomiting	9 (52·9)	7 (41·2)	2 (11·8)	0	0
Leucopenia	6 (35·3)	0	0	3 (17·6)	3 (17·6)
Neutropenia	6 (35·3)	0	0	0	6 (35·3)
Hypokalaemia	6 (35·3)	2 (11·8)	1 (5·9)	2 (11·8)	1 (5·9)
Diarrhoea	5 (29·4)	3 (17·6)	1 (5·9)	1 (5·9)	0
Alanine aminotransferase increased	5 (29·4)	1 (5·9)	1 (5·9)	3 (17·6)	0
Stomatitis	4 (23·5)	1 (5·9)	3 (17·6)	0	0
Nausea	3 (17·6)	3 (17·6)	0	0	0
Lung infection	3 (17·6)	0	1 (5·9)	2 (11·8)	0
Hyperbilirubinaemia	3 (17·6)	2 (11·8)	0	1 (5·9)	0
Arthralgia	3 (17·6)	2 (11·8)	1 (5·9)	0	0
Abdominal pain	2 (11·8)	1 (5·9)	1 (5·9)	0	0
Petechiae	2 (11·8)	1 (5·9)	1 (5·9)	0	0
Skin hyperpigmentation	2 (11·8)	1 (5·9)	1 (5·9)	0	0
Sepsis	2 (11·8)	0	0	1 (5·9)	1 (5·9)
Hypoalbuminaemia	2 (11·8)	1 (5·9)	0	1 (5·9)	0
Hypomagnesaemia	2 (11·8)	2 (11·8)	0	0	0
Hyponatraemia	2 (11·8)	1 (5·9)	0	1 (5·9)	0
Cholestasis	2 (11·8)	0	0	2 (11·8)	0
Allergic transfusion reaction	2 (11·8)	1 (5·9)	1 (5·9)	0	0
Tachycardia	2 (11·8)	2 (11·8)	0	0	0
Headache	2 (11·8)	1 (5·9)	0	1 (5·9)	0

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