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Evaluating Vyxeos use in routine clinical practice; data from the South East Scotland Cancer Network

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SCAN
South East Scotland Cancer Network

INTRODUCTION

Acute myeloid leukaemia (AML) encompasses a group of aggressive haematological neoplasms. It is a clinically, morphologically and genetically heterogeneous disease involving one or all of the myeloid lineages and the most common malignant myeloid disorder in adults. Many factors, both of the disease and the patient, govern treatment decisions and prognosis.

VYXEOS

Vyxeos is a liposomal, synergistic, fixed combination of cytarabine and daunorubicin, preferentially taken up by leukaemic cells within the bone marrow for a prolonged period of time.

Phase III data from the 301 study, showed Vyxeos to improve median overall survival compared to conventional intensive treatment in older patients (60-75 years) with poor risk AML (p=0.003), led to NICE and SMC approval of Vyxeos as a treatment option for untreated therapy-related AML and AML with MDS-related changes (12/2018 and 03/2019 respectively)[1,2]. We undertook a review of patients treated with Vyxeos following SMC approval within the Haematology South East Scotland Cancer Network (SCAN) to assess its safety and efficacy in routine clinical practice.

PATIENT CHARACTERISTICS

9 patients were retrospectively identified as having been treated with Vyxeos from SCAN Multidisciplinary Meeting records. The median time at census post diagnosis was 159 days (range 28-529). The data collected included demographics, diagnostics, treatment and outcomes.

The median age at diagnosis was 61 years (range 17 – 70 years), with n=3 female.

Two were diagnosed with therapy-related AML (22.2%). Six patients (66.7%) had a diagnosis of AML with myelodysplasia-related changes; three had preceding MDS (two had received Azacitidine), one had preceding CMML. One patient was diagnosed with rapidly evolving high-risk MDS, where bone marrow blasts reached 20% at the time of treatment.

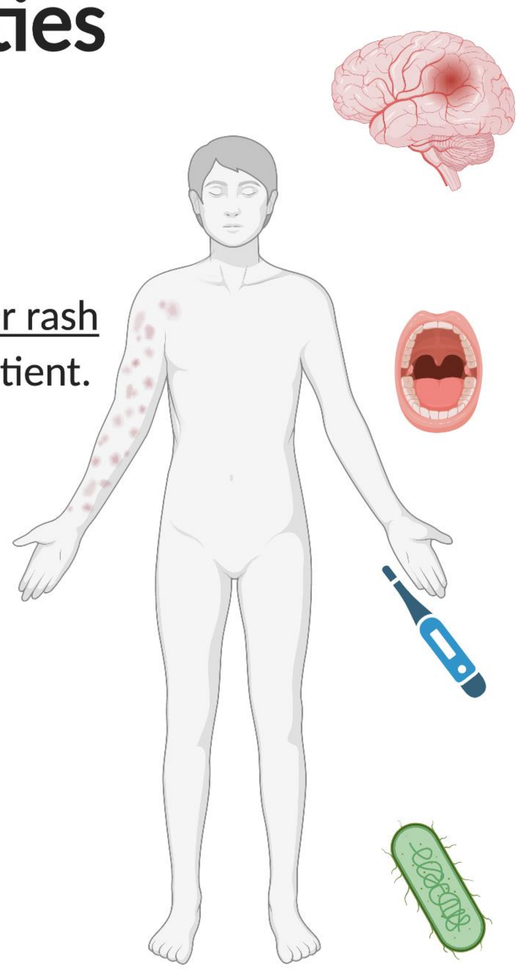
A complex karyotype was observed in two cases, with monosomy 7 found in a third case. Dysplasia was seen in ≥ 2 lineages in all cases. The final patient had refractory *FLT3* positive AML.

The mean white cell count prior to treatment was $27.3x10^9$/l (range $2.6x10^9$/l – $113x10^9$/l) with a mean bone marrow blast percentage of 48% (range 20%-94%) for patient with AML. All had a good performance status (0-1) with no significant co-morbidities.

CONCLUSIONS

This small cohort represents a diverse sample of intensively treated AML patients and our early experience with Vyxeos. Toxicities, early mortality, and remission rates were consistent with the pivotal trial results. Our use of Vyxeos did not raise any unique issues compared with other intensive chemotherapy regimens for AML. Given its proven efficacy in this patient group Vyxeos will no doubt remain a useful weapon in our ever-expanding armoury of AML therapies.

Toxicities



<u>Clinically significant bleeding</u> occured in 3 patients; including 1 intracranial haemorrhage.

<u>Diffuse follicular rash</u> occured in 3 patient.

<u>Severe mucositis</u> occured in 1 patient (grade 3 or above).

<u>Infusion related pyrexia</u> occured in 5 patients.

<u>Neutropenic sepsis</u> occured in 4 patients, two of whom required critical care. One patient died of pneumonia following neutrophil recovery.

OUTCOME DATA

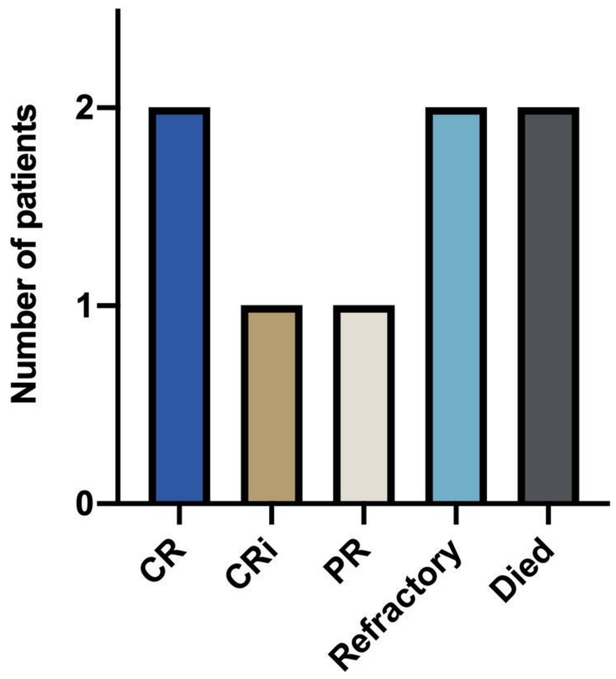


Figure 1. AML response following first cycle Vyxeos. Two patients died before bone marrow assessment; one from intracranial haemorrhage and one from pneumonia following neutrophil recovery.

Toxicities encountered, illustrated above, during Vyxeos treatment in our small cohort of patients was largely consistent with expectations for intensive AML therapy.

Neutrophil recovery took on average 27 days (range 19-39 days). Platelet recovery took longer, on average 33 days (range 25-59 days) with one patient who did not achieve platelet recovery.

Bone marrow response assessments for those treated for AML following first cycle Vyxeos are shown in Figure 1.

Following recovery from cycle 1, four patients received a second cycle of Vyxeos. One of theses patients proceeded to allogenic bone marrow transplant. One patient received a single cycle of Vyxeos and proceeded to allogenic bone marrow transplant. Both transplanted patients remain in remission to date.

Of the three non-transplanted patients who received a second cycle of Vyxeos, two patients relapsed during recovery from their second cycle and one remained in remission with incomplete haematological recovery. An attempt at further induction was made in one of the relapsed patients with high dose cytarabine followed by FLAG-Ida, unfortunately this was unsuccessful in achieving remission.

Of the two refractory cases, one patient was managed symptomatically and the other received compassionate use quizartinib.

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