

[115] SURVIVAL AND EFFICACY OF DECITABINE IN MYELOYDYSPLASTIC SYNDROMES (MDS), ANALYSIS OF THE 5-DAY IV DOSING REGIMEN

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An optimized dosing regimen for decitabine, an epigenetic therapy approved for the treatment of MDS, has been described recently based on the results of a single center, Phase II three arm adaptive randomization study (Kantarjian *et al*, Cancer 2007;109:265-273). The results of this trial have been described in the context of a pooled data set from all three treatment arms; only a limited set of data specific to the 5-day IV dosing arm has been presented. Here, we provide an in-depth update of important efficacy and toxicity endpoints specific to the 93 patients treated within this trial with the 5-day schedule. 39/93 patients were not categorized (N/C) by IPSS due to exclusion from IPSS (extensive prior therapy, secondary MDS). Distribution by IPSS in the 54 categorized patients was: Intermediate-1

(INT-1) 26%, Intermediate-2 (INT-2) 50%, and High risk (HR) 24%. The median age was 65 years (range 37-83). Abnormal chromosomes were observed in 62%, 47% had >10% bone marrow blasts; 96% had various degrees of cytopenias. Secondary MDS was documented in 28 patients (30%). The median duration of MDS was 2.5 months. Prior therapy for MDS was given to 52 pts (56%): growth factors only in 34; chemotherapy \pm growth factors 18. Overall 36 pts (39%) pts achieved CR, and 75 (81%) had a response by IWG criteria. The response rates by IWG criteria with IPSS subsets were: INT-1 71% (9 CR, 1 marrow CR); INT-2 70% (9 CR, 6 hematologic improvement [HI], 4 marrow CR); HR 62% (4 CR, 3 HI, 1 marrow CR); and N/C 72% (14 CR, 1 PR, 6 HI, 7 marrow CR). The median number of cycles was 8+. The

median time to response was 2.3 months. The median duration of CR was 14 months (range 3 to 16+ months). The median time to acute myeloid leukemia (AML) transformation or death was 15 months. The median time to AML (censoring for death without AML) was 30 months. The median survival was 20 months, with 1- and 2-year survival rates of 61% and 41%, respectively. The side effect profile for the 5-day IV regimen was consistent with what has been previously reported, with Grade 3-4 drug-related extramedullary side effects being uncommon. The encouraging survival and response rates of the 5-day dosing regimen of decitabine in this poor-prognosis population, coupled with its manageable side effect profile, provide a beneficial therapeutic option and a foundation for further advances for patients with MDS. *

[29] EFFICACY OF NILOTINIB (AMN107) IN PATIENTS (PTS) WITH NEWLY DIAGNOSED, PREVIOUSLY UNTREATED PHILADELPHIA CHROMOSOME (PH)-POSITIVE CHRONIC MYELOGENOUS LEUKEMIA IN EARLY CHRONIC PHASE (CML-CP).

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Background

Nilotinib is a novel, oral tyrosine kinase inhibitor with increased selectivity against Bcr-Abl that is approximately 30-fold more potent than imatinib. High response rates have been reported with nilotinib therapy in CML after imatinib failure.

Methods

We evaluated the efficacy of nilotinib

as first line therapy in pts with newly diagnosed Ph-positive CML-CP. The primary objective was to estimate the proportion of pts attaining major molecular response (BCR-ABL/ABL ratio \leq 0.05% in our lab) at 12 months (mo).

Results

Thirty-two pts have been treated with nilotinib 400 mg orally twice daily

for a median of 5 months (mo) (range, 1 to 31 mo). The median age was 47 years (yrs) (range, 24-73 yrs). The Sokal risk at pretreatment was low in 21 (70%) pts, intermediate in 6 (20%), and high in 3 (10%). The rate of complete cytogenetic response [CCyR] (Ph 0%) at 3, 6 and 12 mo compares favorably to those observed in historical controls treated with imatinib

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