INTERVIEW

David P Steensma, MD

Dr Steensma is Attending Physician at the Dana-Farber Cancer Institute and Associate Professor of Medicine at Harvard Medical School in Boston, Massachusetts.

Tracks 1-12

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Tracks 2-3

DR LOVE: Would you comment on the poster presented at ASH 2009 on the AVIDA registry that compared dosing regimens and the efficacy of subcutaneous versus intravenous azacitidine for myelodysplastic syndromes (MDS)?

DR STEENSMA: What I found interesting about the IV versus subcutaneous azacitidine comparison was that the response rates, in terms of hematologic improvement, were identical (Sekeres 2009). So although the AZA-001 study, which showed a survival advantage with azacitidine in high-risk MDS, used subcutaneous administration (Fenaux 2010), I believe that IV administration is acceptable and avoids some of the potential difficulties with subcutaneous administration, such as skin reactions.

The study also revealed that the vast majority of patients are not receiving the FDA-approved seven consecutive days of azacitidine. Perhaps that is not surprising, but what is alarming is that approximately 50 percent of patients are not even receiving this agent for a total of seven days per cycle. Many clinicians administer it for five days one week and two the next, but some administer it for only five days.

Data from the Spanish Azacitidine Compassionate Use Registry, also reported at ASH 2009, showed that the complete response rate was 12 percent for patients who received azacitidine on fewer than seven days per cycle and 22 percent for those who received it for seven days per cycle (Garcia 2009). It was a small retrospective study, but I believe that we should do our best to administer azacitidine for seven days.

DR LOVE: For how long should patients with MDS continue to receive treatment?

DR STEENSMA: We don't have clinical trial data to answer that question. For patients who demonstrate a complete response, I use maintenance therapy because it has been my experience that if I administer only two more cycles and then stop, as I do for lymphoma cases, the vast majority of patients experience relapse within six months. Varying opinions exist in terms of the best way to administer maintenance therapy. My practice with both azacitidine and decitabine is to wait six or seven weeks between cycles. Others decrease the dose, reducing azacitidine from 75 to 50 mg/m^2 or decitabine from 20 to 10 mg/m^2 and administering it for five days.

Tracks 5-6

DR LOVE: Would you discuss the data and clinical implications of the MDS-004 study that was presented at ASH 2009?

DR STEENSMA: This Phase III study compared five- or 10-mg lenalidomide to placebo for patients with low-risk or intermediate-1-risk MDS with 5q deletion. The complete cytogenetic response rate was more than twice as high on the 10-mg arm, and although the differences between the two doses weren't statistically different, the trend favored the higher dose (Fenaux 2009; [2.1]).

The incidence of cytopenias was approximately the same, with 58 percent of the patients who received the higher dose and 52 percent on the 5-mg arm requiring dose reduction. In most patients it is fairly well tolerated — certainly better than thalidomide. I believe that the starting dose of lenalidomide should be 10 mg, even for older patients.

Tracks 11-12

DR LOVE: What is the current approach to induction therapy for acute promyelocytic leukemia (APL)?

DR STEENSMA: Generally, the trend has been away from cytarabine and toward incorporating the three most active agents — arsenic trioxide, tretinoin and gemtuzumab — earlier in therapy. The Intergroup study in higher-risk APL, SWOG-S0535, is evaluating all three agents as induction therapy, which is an exciting approach.

DR LOVE: What is your initial approach to treating APL in practice?

DR STEENSMA: Outside a protocol setting, I believe the PETHEMA regimen or the older CALGB regimen that includes arsenic trioxide early, an anthracycline and then the incorporation of arsenic trioxide in one or more consolidation therapies is the best approach.

If I were diagnosed with APL, I would want to receive both tretinoin and arsenic trioxide at some point, and preferably — particularly with higher-risk disease — gemtuzumab, which is another active agent in APL. ■

2.1

MDS-004: Efficacy and RBC Transfusion Independence (TI) with Lenalidomide Five or 10 Mg versus Placebo in Patients with Low- or Intermediate-1-Risk Myelodysplastic Syndromes and the 5q Deletion

	Placebo	Lenalidomide 5 mg	Lenalidomide 10 mg
Protocol RBC TI (≥26 weeks)	6%	41%[1]	56%[1]
IWG RBC TI (≥8 weeks)	8%	50%[1]	61%[1]
Median time to protocol TI (≥26 weeks)	0.3 weeks	3.3 weeks	4.3 weeks
Median maximum hemoglobin increase	2.3 g/dL	5.1 g/dL[2]	6.3 g/dL[3]
Complete CyR + partial CyR	0%	17%[1]	41%[1]
Complete CyR	0%	11%[3]	24%[1]

IWG = International Working Group consensus criteria; CyR = cytogenetic response
[1] $p < 0.001$ versus placebo; [2] $p < 0.05$ versus placebo; [3] $p = 0.01$ versus placebo

Fenaux P et al. *Proc ASH* 2009;**Abstract 944**.

SELECT PUBLICATIONS

Fenaux P et al. **Prolonged survival with improved tolerability in higher-risk myelodysplastic syndromes: Azacitidine compared with low dose ara-C.** *Br J Haematol* 2010;149(2):244-9.

Fenaux P et al. **RBC transfusion independence and safety profile of lenalidomide 5 or 10 mg in pts with low- or int-1-risk MDS with del5q: Results from a randomized Phase III trial (MDS-004).** ASH 2009;**Abstract 944**.

Garcia R et al. **Different clinical results with the use of different dosing schedules of azacitidine in patients with myelodysplastic syndrome managed in community-based practice: Effectiveness and safety data from the Spanish Azacitidine Compassionate Use Registry.** *Proc ASH* 2009;**Abstract 2773**.

Sekeres MA et al. **A study comparing dosing regimens and efficacy of subcutaneous to intravenous azacitidine (AZA) for the treatment of myelodysplastic syndromes (MDS).** *Proc ASH* 2009;**Abstract 3797**.