INTERVIEW

Steven D Gore, MD

Dr Gore is Professor of Oncology at Johns Hopkins University in Baltimore, Maryland.

Tracks 1-14

Select Excerpts from the Interview

Tracks 5-9

DR LOVE: How are you generally approaching patients with higher-risk myelodysplastic syndromes (MDS) or those with chromosome 5q deletion?

DR GORE: My first question is always, is this patient now or could this patient ever be a candidate for a potentially curable allogeneic stem cell transplant? That always needs to be kept in mind. We perform nonablative transplants up through age 75, so it's not a trivial question. That's not to say that every 75-year-old should undergo a transplant, but it could be considered for

appropriate patients up through that age. Patients at higher risk should start a nucleoside analog, and the only one that has been proven to improve survival is azacitidine (Fenaux 2009).

For patients at lower risk whose disease has failed to respond to or who are not candidates for erythropoietin-stimulating agents and who have deletion of chromosome 5q, lenalidomide is the treatment of choice. For patients who don't have that abnormality, lenalidomide can be considered if they are not thrombocytopenic.

DR LOVE: What are your thoughts on the issue of duration of treatment with hypomethylating agents?

DR GORE: A recently published analysis of the AZA-001 data evaluated time to first response and best response and reported that it may take as long as 12 months to see your first hematologic response, and responses do continue to improve with continued azacitidine therapy (Silverman 2011). For patients with high-risk disease, the current recommendation remains to continue therapy as long as the disease is responding and the patient is tolerating the drug.

Data from four independent cohorts were analyzed with regard to outcomes of patients whose disease either failed to respond to azacitidine or responded and then ceased to respond (Prebet 2010). Patients whose disease stops responding or doesn't respond to azacitidine have a limited life expectancy, so it seems that the longer patients continue to receive it, the better off they are.

Tracks 11-12

DR LOVE: What new developments have occurred recently in acute promyelocytic leukemia (APL)?

DR GORE: The main event this past year was the publication of data from the CALGB-C9710 trial, which randomly assigned patients with APL to standard induction followed by consolidation therapy with or without two cycles of arsenic trioxide (ATO). Survival was markedly improved in the patients

2.1

Intergroup Study C9710: Arsenic Trioxide (ATO) with Standard Induction/Consolidation Therapy* for Acute Promyelocytic Leukemia

Endpoint	Induction → consolidation (n = 237)	Induction → consolidation + ATO† (n = 244)	*p*-value
Three-year event-free survival	63%	80%	<0.0001
Three-year overall survival	81%	86%	0.07
Three-year disease-free survival	70%	90%	<0.0001

* Induction (ATRA, Ara-C, daunorubicin) → two courses consolidation (ATRA, daunorubicin)
† Two 25-day courses of ATO consolidation immediately after induction

Powell BL et al. *Blood* 2010;116(19):3751-7.

receiving ATO (Powell 2010; [2.1]). The CALGB-C9710 study has been criticized because event-free survival on the control arm was only about 60 percent, which is not great compared to results from the Spanish PETHEMA group trial (Ades 2008; Gore 2010). With that said, this was a well-done randomized clinical trial consistent with other recent APL studies (2.2), and I believe these are real data that illustrate the importance of ATO in this setting.

Another interesting aspect is that ATO seems to overcome the negative effect of high-risk APL. The outcomes for patients on the CALGB-C9710 trial with high-risk APL who receive ATO, once they're in remission, are comparable to the outcomes for patients with low-risk APL. Virtually no relapses occur in patients who survive APL and receive arsenic-based therapy (Powell 2010). ■

2.2 **Comparison of Outcomes in Recent Trials for Acute Promyelocytic Leukemia**

	Gore 2010[1] (n = 45)	C9710 ATO arm[2] (n = 243)	PETHEMA LPA99[3] (n = 410)	APL2000 Ara-C arm[4] (n = 178)	Shanghai[5] (n = 85)	MD Anderson[6] (n = 82)
OS	88%	86%	93.7%	90.5%	91.7%	84.1%
DFS	90%	90%	NR	NR	94.8%	90.6%
EFS	76%	80%	86%	85.6%	89.2%	82.9%
Follow-up	2.7 y	2.4 y	5.6 y	5.2 y	5.8 y	1.9 y

[1] ATRA + DNR → cytarabine + DNR → 30 doses ATO beginning on day 8; [2] (ATRA, Ara-C, DNR) → two courses (ATRA, DNR) → two 25-day courses ATO; [3] ATRA, high cumulative dose idarubicin and mitoxantrone; [4] Ara-C + ATRA + lower cumulative dose DNR; [5] ATRA/ATO-based therapy; [6] ATRA, ATO, gem

ATO = arsenic trioxide; OS = overall survival; DFS = disease-free survival; NR = not reported; EFS = event-free survival; ATRA = all-trans retinoic acid; DNR = daunorubicin; gem = gemtuzumab

Gore SD et al. *J Clin Oncol* 2010;28(6):1047-53; Powell BL et al. *Blood* 2010;116(19):3751-7.

SELECT PUBLICATIONS

Ades L et al. **Treatment of newly diagnosed acute promyelocytic leukemia (APL): A comparison of French-Belgian-Swiss and PETHEMA results.** *Blood* 2008;111(3):1078-84.

Fenaux P et al. **Efficacy of azacitidine compared with that of conventional care regimens in the treatment of higher-risk myelodysplastic syndromes: A randomised, open-label, phase III study.** *Lancet Oncol* 2009;10(3):223-32.

Gore SD et al. **Single cycle of arsenic trioxide-based consolidation chemotherapy spares anthracycline exposure in the primary management of acute promyelocytic leukemia.** *J Clin Oncol* 2010;28(6):1047-53.

Powell BL et al. **Arsenic trioxide improves event-free and overall survival for adults with acute promyelocytic leukemia: North American Leukemia Intergroup study C9710.** *Blood* 2010;116(19):3751-7.

Prebet T et al. **Outcome of patients (pts) treated for myelodysplastic syndrome (MDS) and secondary acute myeloid leukemia (s AML) after azacitidine (AZA) failure.** *Proc ASH* 2010;**Abstract 443**.

Silverman LR et al. **Continued azacitidine therapy beyond time of first response improves quality of response in patients with higher-risk myelodysplastic syndromes.** *Cancer* 2011;[Epub ahead of print].