

To: Johanna Clifford, RN, MSN
Health Science Administrator for the Oncology Drugs Advisory
Committee
Advisors and Consultants Staff

From: Ann T. Farrell, MD
Clinical Team Leader
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Re: Errata in FDA Genasense Briefing Document

Date: April 26, 2004

The following errata have been discovered and need to be corrected in the FDA Genasense Briefing Document.

Page 14, Paragraph 4, line 3

There is a typo. The following sentence is incorrect:
One hundred U.S. sites enrolled 54% of the patients.

and should read:
One hundred U.S. sites enrolled 56% of the patients.

Page 18: 2nd line from the bottom

Original: ... 65 cm versus 75 cm ...

Revised: ... 65 mm versus 75 mm ...

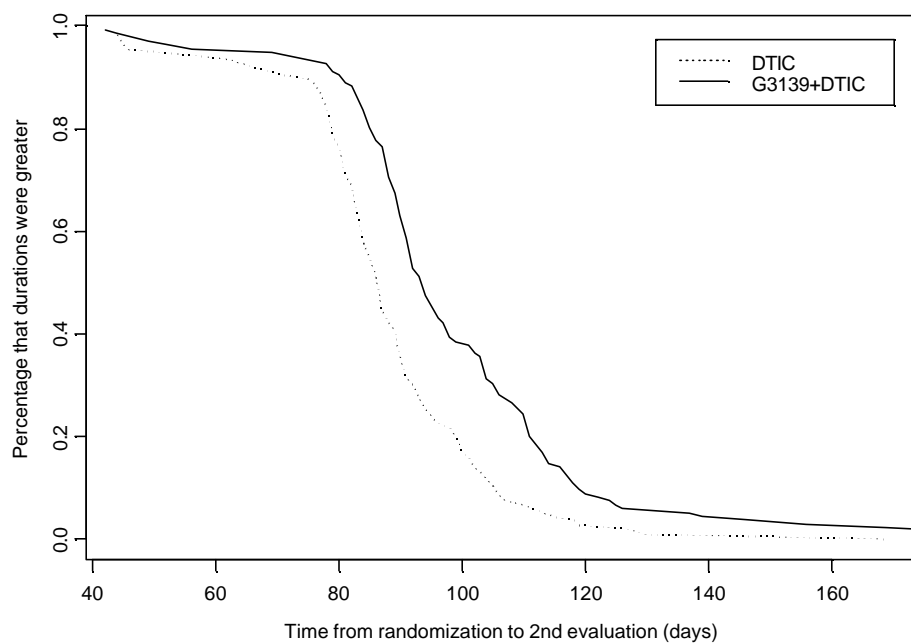
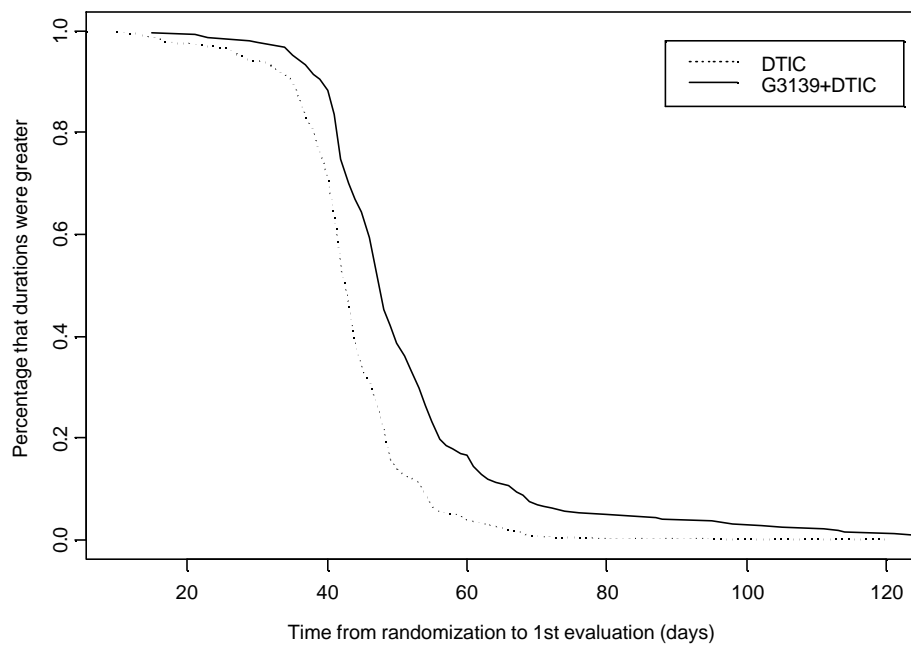
Page 20, Table 6

There is a typo. In the row labeled "Death" in the cell under the column labeled "DTIC alone" the number should be 15 instead of 1.

Pages 31 and 33: Dotted curves in Figures 6 and 7 are not visible in the original document. Enlarged figures are provided as below.

Figure 6: Kaplan-Meier Curves of Time from Randomization to 1st, 2nd, and 3rd Lesion Assessments (Reviewer's Figures)

[**Note:** Assessments conducted after the date of documented disease progression or death were excluded.]



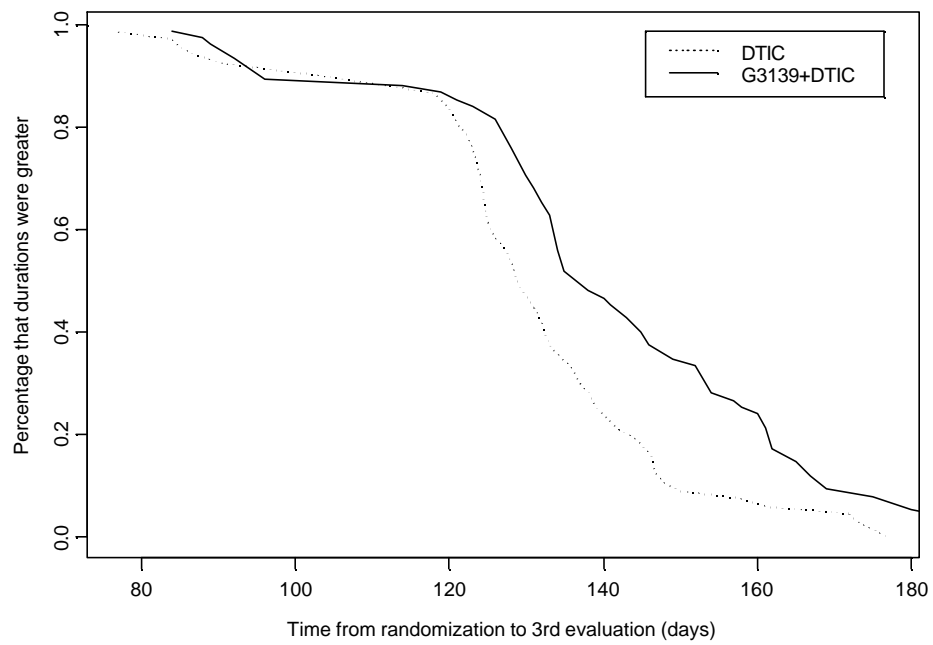
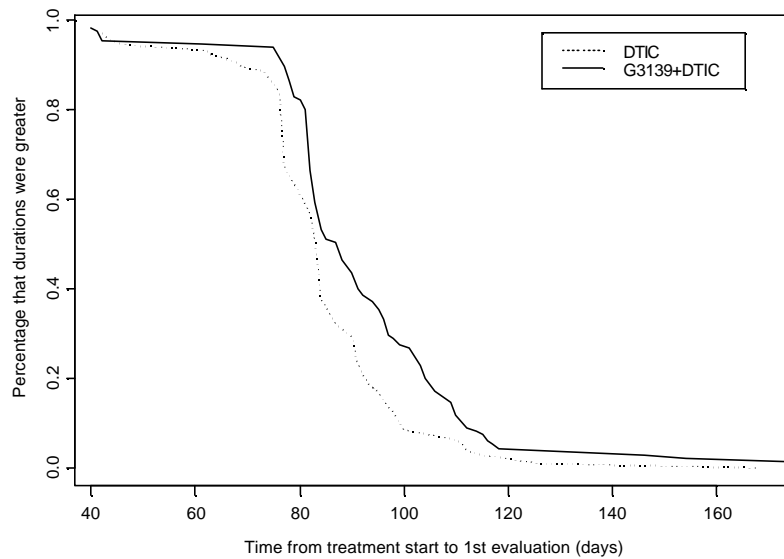
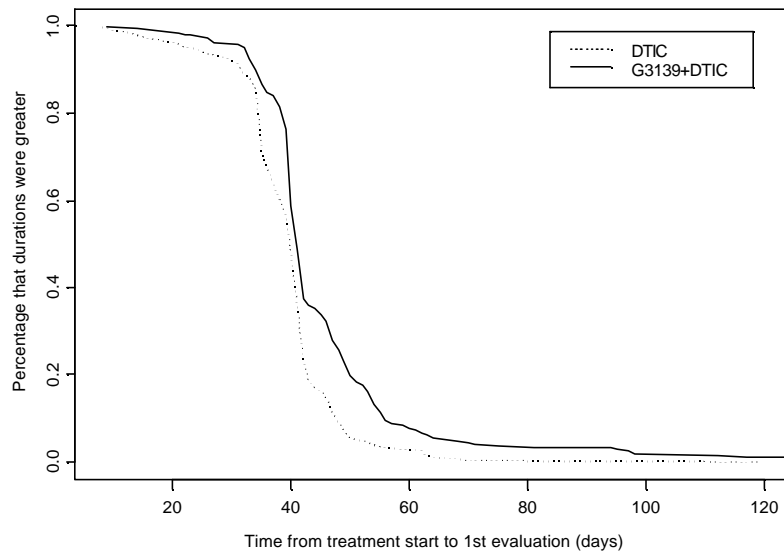
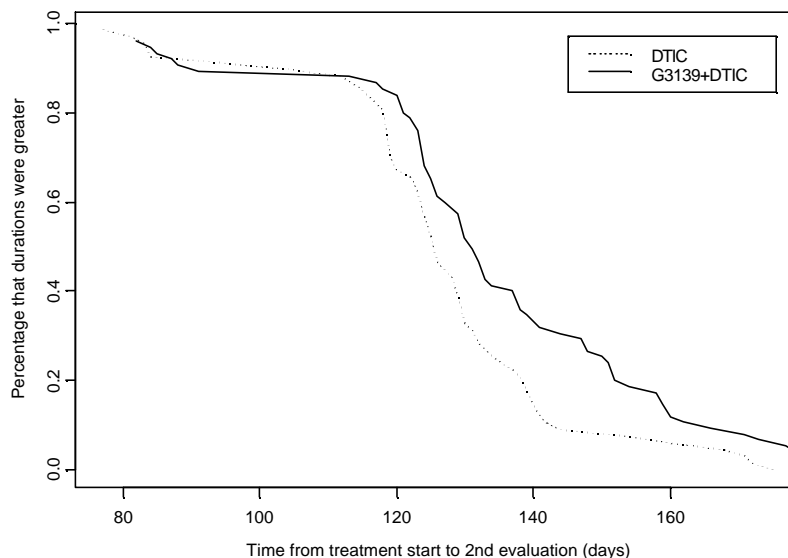


Figure 1: Kaplan-Meier Curves of Time from Treatment Start to 1st, 2nd, and 3rd Lesion Assessment (Reviewer's Figures)

[Note: Assessments after documented disease progression or death were excluded from the analysis.]





Pages 36-37: Tables 17-19 in the original document are to be replaced by the following three tables. Numbers referred in the text should be changed accordingly.

Table 17: Summary of Number of Patients with Missing Lesion Measurements Prior to Documented Disease Progression or Death Among Those Who Had Disease Progression or Death (Reviewer's Table)

Lesions	Missing at Least One Lesion Measurement		Missing More Than 50% of Lesion Measurements	
	G3139 + DTIC [N = 263] [†]	DTIC [N = 260] [†]	G3139 + DTIC [N = 263] [†]	DTIC [N = 260] [†]
Target	16 (6.1%)	13 (5.0%)	6 (2.3%)	2 (0.8%)
Non-target	90 (34.2%)	69 (26.5%)	46 (17.5%)	37 (14.2%)
Target or nontarget	91 (34.6%)	69 (26.5%)	46 [‡] (17.5%)	37 [‡] (14.2%)

[†] Number of patients who had disease progression or death in each treatment group.

[‡] Number of patients who had more than 50% of missing target lesion measurements or more than 50% of missing nontarget lesion measurements.

Table 18: Summary of Number of Patients with Missing Lesion Measurements First Occurred at The Same Time of Documented Disease Progression or Death Among Those Who Had Disease Progression or Death (Reviewer's Table)

Lesions	Missing at Least One Lesion Measurement		Missing More Than 50% of Lesion Measurements	
	G3139 + DTIC [N = 263] [†]	DTIC [N = 260] [†]	G3139 + DTIC [N = 263] [†]	DTIC [N = 260] [†]
Target	30 (11.4%)	25 (9.6%)	6 (2.3%)	6 (2.3%)
Non-target	126 (47.9%)	137 (52.7%)	43 (16.3%)	49 (18.8%)
Target or nontarget	131 (49.8%)	145 (55.8%)	47 [‡] (17.9%)	53 [‡] (20.4%)

[†] Number of patients who had disease progression or death in each treatment group.

[‡] Number of patients who had more than 50% of missing target lesion measurements or more than 50% of missing nontarget lesion measurements.

Table 19: Summary of Number of Patients with Missing Lesion Measurements Among Those Who Were Censored and Had Baseline and Post Baseline Target Lesion Measurements (Reviewer's Table)

Lesions	Missing at Least One Lesion Measurement		Missing More Than 50% of Lesion Measurements	
	G3139 + DTIC [N = 58] [†]	DTIC [N = 51] [†]	G3139 + DTIC [N = 58] [†]	DTIC [N = 51] [†]
Target	7 (12.1%)	7 (13.7%)	3 (5.2%)	3 (5.9%)
Non-target	55 (94.8%)	45 (88.2%)	37 (63.8%)	25 (49.0%)
Target or nontarget	55 (94.8%)	45 (88.2%)	37 [‡] (63.8%)	25 [‡] (49.0%)

[†] Number of censored patients who had baseline and post baseline lesion measurements in each treatment group.

[‡] Number of patients who had more than 50% of missing target lesion measurements or more than 50% of missing nontarget lesion measurements.

Page 38

There is a typo. The following sentence is incorrect:

Especially, when taking into account missing nontarget lesion measurements (Approaches 3 and 4) there is no statistically significant difference in progression-free survival between treatment groups at the significance level of 0.05.

and should read:

Especially, when taking into account missing nontarget lesion measurements (Approach 4) there is no statistically significant difference in progression-free survival between treatment groups at the significance level of 0.05.

Page 39: Table 21 in the original document is to be replaced by the following table.

Table 21: Results of Generalized Logrank Test with Interval-Censored Data (Reviewer's Table)

Approach	Estimated Median (days)		P value from two-sided generalized logrank test
	G3139 + DTIC	DTIC	
1	22	2	0.016
2	10	2	0.026
3	10	2	0.031
4	10	2	0.141

Note: P-value was from generalized logrank test comparing the entire curves between the two treatment groups.

Page 40, Table 23

There is a typo. The p-value for the difference in proportions should read 0.052 not 0.52.

Page 45, Table 30

There is a typo. In the row labeled "Non-US Median Survival Time" in the cell under the column labeled "DTIC alone" the number should be 213 instead of 123.

Page 46, Table 33

There is a typo. In the row labeled "Median" in the cell under the column labeled "DTIC alone" the number should be 2008.1 instead of 2009.1.

Pages 53-54: Tables 38-39 in the original document are to be replaced by the following two tables.

Table 38: Assessment Schedules in Simulation Studies (Reviewer's Table)

Configuration	Control Group	Experimental Group
1A	Days 42, 84, 126, 168, 210, 252	(delayed by 2 days) Days 44, 86, 128, 170, 212, 254
1B	Same as above	(assessment interval 2 days longer) Days 44, 88, 132, 176, 220, 264
2A	Days 21, 42, 63, 84, 105, 126, 147, 168, 189, 210, 231, 252	(delayed by 2 days) Days 23, 44, 65, 86, 107, 128, 149, 170, 191, 212, 233, 254
2B	Same as above	(assessment interval 2 days longer) Days 23, 46, 69, 92, 115, 138, 161, 184, 207, 230, 253, 276

Table 39: Simulation Results under Equal Progression-Free Survival Distributions (Reviewer's Table)

(Monte Carlo Estimates Based on 5000 Replications)

Configuration	Sample size per treatment group	Median (days)		Probability of false inference [†]	Logrank P-value [‡]
		G3139 + DTIC	DTIC		
1A	100	86	84	0.66	0.094
	300	86	84	0.98	0.004
1B	100	88	84	0.60	0.114
	300	88	84	0.97	0.007
2A	100	65	63	0.18	0.358
	300	65	63	0.41	0.198
2B	100	69	63	0.10	0.427
	300	69	63	0.21	0.330

[†] The probability of false inference was estimated by the proportion of the 5000 replications where the null hypothesis was rejected. This represented the probability of falsely inferring a difference in progression-free survival between the two treatment groups.

[‡] This was the average of 5000 p-values. Each simulation produced a p-value. These p-values were from two-sided logrank test comparing progression-free survival between treatment groups.