

FDA's Efalizumab Briefing Book – Revisions to text and tables

Page 33, paragraph 1, last sentence: Change "84-day" to "168-day".

Page 87, last bullet point: Replace the sentence:

In patients who were nonresponders or partial responders during the first 12 weeks of efalizumab treatment, extended treatment with a contiguous 3 month treatment course can result in an additional 11%-14% PASI 75 response (depending on the study).

with the following sentence:

In study ACD2059g, in patients who were nonresponders during the first 12 weeks of efalizumab treatment, extended treatment with a contiguous 3-month treatment course at a higher than proposed dose (4 mg/kg/wk) resulted in an additional 11% PASI 75 response over placebo.

Page 93, Table 68, title, change, "... (Studies 2058, 2059, and 2390)..." to, "... (Studies 2600, 2058, 2059, and 2390)..."

Page 94, paragraph 1, line 2, change: "...1.08..." to, "1.18".

Page 97, Table 70, row 23 (moniliasis), change: "5 (0.3%)" to, "6 (0.3%)".

Page 105, paragraph 4, line 7, change: "...67,000/mm3..." to, "...60,000/mm3..."

Page 105, paragraph 5, line 3, change: "...2002..." to, "...2000..."

Page 106, paragraph 3, line 5, change: "...6,000 cell/mm3..." to, "...33,000 cells/mm3..."

Page 115, paragraph 4, line 2, change: "...efalizumab..." to, "...placebo..."

Page 115, paragraph 4, line 3, change: "...January 15, 2003..." to, "...January 15, 2001..."

Page 115, paragraph 4, line 8, change: "...February 26, 2003..." to, "March 15, 2001..."

Page 118, paragraph 1, line 2, change: "...headache, chills, fever, and myalgia." To, "headache and chills".

Page 127, Section 10, paragraph 3, line 3, change: "(19%-26%)" to "(16%-29%)".

Page 127, Section 10, paragraph 6, line 2, change (11-14%) to (up to 11% with the 4 mg/kg/wk dose).

FDA's Efalizumab Briefing Book – Updated tables

Page 94, changes (blue) to Table 69 is provided.

Table 69 Incidence Rate for Infection that Required Hospitalization Total Exposure All Patients by Treatment Group

Treatment Group	Number of Events	Subject-Years	95% CI for Observed Number of Events	Incidence Rate Per 100 Subject-Years	95% CI for Incidence Rate Per 100 Subject-Years
Efalizumab	27	1680	[17.79, 39.28]	1.61	[1.06, 2.34]
Placebo	2	169.48	[0.24, 7.22]	1.18	[0.14, 4.26]

Page 107, an updated Table 78 is provided below.

Table 78 Psoriasis Flares and Variants Reported for First Exposure, Controlled Period (XOMA and GNE)

Adverse Event	Placebo 715	All Efalizumab 1620
Subjects with psoriasis AEs	10 (1.4%)	52 (3.2%)
Psoriatic erythroderma	(0.0%)	9 (0.6%)
Pustular psoriasis	(0.0%)	4 (0.2%)
Guttate psoriasis	2 (0.3%)	19 (1.2%)
Recurrence of plaque psoriasis	6 (0.8%)	9 (0.6%)
Unusual morphology	2 (0.3%)	6 (0.4%)
Inverse psoriasis	(0.0%)	5 (0.3%)
Palmo-plantar psoriasis	(0.0%)	4 (0.2%)

Page 108, an updated Table 79 is provided below.

Table 79 Serious Adverse Events of Psoriasis Flares Experienced by Subjects Treated with Efalizumab

Subject ID	Event	Exposure Period	Response to Treatment	Admitted to Hospital
25609	Erythroderma	FE	NR	Yes
16513	Erythroderma	EE	NR	Yes
82009	Exfoliative erythroderma	EE	Initial R, then lost efficacy to NR	Yes
16517	Erythroderma	RE	PR	Yes
19515	Erythroderma	WO	NR	Yes
21505	Erythrodermic pustular	WO	R	Yes
25906	Pustular von Zumbusch	WO	NR	No
27708	Pustular	WO	PR initially then lost efficacy to NR	Yes
64006	Flare	WO	NR	Yes
82024	Erythroderma	WO	R	Yes
12516	Pustular	Post-WO	NR	Yes
16533	Erythroderma	NC ^a	NR	Yes
25914	Pustular von Zumbusch	Post-WO	PR initially then lost efficacy to NR	No
28615	Pustular	Post-WO	R	No
80002	Atypical flare	Post-WO	NR	Yes
16511	Erythroderma	NC ^a	NR	Yes
25601	Psoriasis Flare	WO	R	Yes
31614	Erythrodermic Psoriasis	WO	NR	Yes
32802	Worsening of Psoriasis	ET	NR	Yes

NC=not classified; NR=non-responder or non-response; PR=partial responder; R=responder. WO= washout; FE= first exposure; EE= extended treatment

^a The event occurred approximately 4 weeks after early discontinuation from FE. The subject had received three doses of efalizumab. The case was also counted during WO.

Page 111, an updated Table 80 is provided below.

Table 80 Severe Non-Serious Adverse Events of Erythrodermic or Pustular Psoriasis Reported for Efalizumab-Treated Subjects

Subject ID	Event	Exposure Period	Response to Treatment	Intensity
82026	Erythroderma	FE	NR	Severe
34229	Erythroderma	FE	NR	Severe
75610	Erythroderma	FE	NR	Severe
79202	Pustules in groin	FE	PR	Severe
69202	Erythroderma	WO	R	Severe
79208	Pustular lesions on groin/buttocks	WO	PR initially then lost efficacy to NR	Severe
80811	Erythroderma	WO	R	Severe
82003	Erythroderma	WO	PR	Severe
18503	Erythroderma	WO	NR	Severe
31403	Erythroderma	FE	NR	Severe
34229	Erythroderma	FE	NR	Severe
43409	Erythroderma	FE	NR	Severe
46410	Erythroderma	FE	NR	Severe

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Page 117, an updated Table 83 is provided below

Table 83 Adverse Events that Occurred in $\geq 3\%$ of Subjects Treated with Genentech Material in the 1.0 mg/kg/wk Group or the Placebo Group in the FE/Controlled Studies

COSTART Body System/ Preferred Term	Genentech Efalizumab		
	Placebo (n=455)	1.0 mg/kg/wk (n=869)	2.0 mg/kg/wk (n=61)
Subjects with at least one adverse event	328 (72.1%)	707 (81.4%)	56 (91.8%)
Body as a whole			
Headache	86 (18.9%)	276 (31.8%)	18 (29.5%)
<i>Infection</i>	76 (16.7%)	120 (13.8%)	14 (23.0%)
Chills	19 (4.2%)	104 (12.0%)	8 (13.1%)
Pain	20 (4.4%)	73 (8.4%)	9 (14.8%)
Flu syndrome	20 (4.4%)	74 (8.5%)	2 (3.3%)
Fever	9 (2.0%)	48 (5.5%)	7 (11.5%)
Asthenia	16 (3.5%)	50 (5.8%)	4 (6.6%)
<i>Accidental injury</i>	32 (7.0%)	42 (4.8%)	5 (8.2%)
Back pain	8 (1.8%)	31 (3.6%)	2 (3.3%)
Digestive			
Nausea	25 (5.5%)	84 (9.7%)	8 (13.1%)
Diarrhea	28 (6.2%)	45 (5.2%)	5 (8.2%)
<i>Gastroenteritis</i>	19 (4.2%)	23 (2.6%)	0
Musculoskeletal			
Myalgia	22 (4.8%)	75 (8.6%)	9 (14.8%)
Arthralgia	10 (2.2%)	27 (3.1%)	4 (6.6%)
Respiratory			
Pharyngitis	29 (6.4%)	67 (7.7%)	5 (8.2%)
Rhinitis	26 (5.7%)	55 (6.3%)	4 (6.6%)

Adverse events with a $\geq 1\%$ higher incidence among the efalizumab-treated patients compared to placebo-treated patients are highlighted in bold.

Page 120, an updated Table 86 is provided below.

Table 86 Change in White Blood Cell Counts (K/cmm) from Baseline to Day 84 of Each Period for Subjects Treated with Genentech Efalizumab

Type of Study/Period	Placebo	Genentech Efalizumab, Mean			
		2.0 mg/kg/qow	1.0 mg/kg/wk	2.0 mg/kg/wk	3.0-4.0 mg/kg/wk
FE/Controlled	-0.09	NA	2.53	3.20	NA
FE	NA	2.17	2.51	2.54	2.53
EE-1	NA	3.03	2.66	2.71	2.72
EE-2	NA	NA	2.71	3.27	2.84
EE-3	NA	NA	2.66	2.72	4.92
EE-4	NA	NA	2.23	2.94	5.23
RE-1	NA	NA	2.40	2.97	NA
WO	NA	0.20	0.06	0.32	0.09

NA=not applicable.

Page 122, an updated Table 89 is provided below.

Table 89 Change in Alkaline Phosphatase (U/L) from Baseline to Day 84 of Each Period for Subjects Treated with Genentech Efalizumab

Type of Study/Period	Placebo	Genentech Efalizumab, Mean			
		2.0 mg/kg/qow	1.0 mg/kg/wk	2.0 mg/kg/wk	3.0-4.0 mg/kg/wk
FE/Controlled	-1.03	NA	5.29	9.57	NA
FE	NA	-1.3	5.5	11.1	23.2
EE-1	NA	9.27	7.48	33.40	0.87
EE-2	NA	NA	7.97	13.54	9.25
EE-3	NA	NA	6.92	11.98	12.00
EE-4	NA	NA	9.39	9.28	15.50
RE-1	NA	NA	14.43	8.63	NA
WO	NA	0.95	0.46	5.21	-1.42