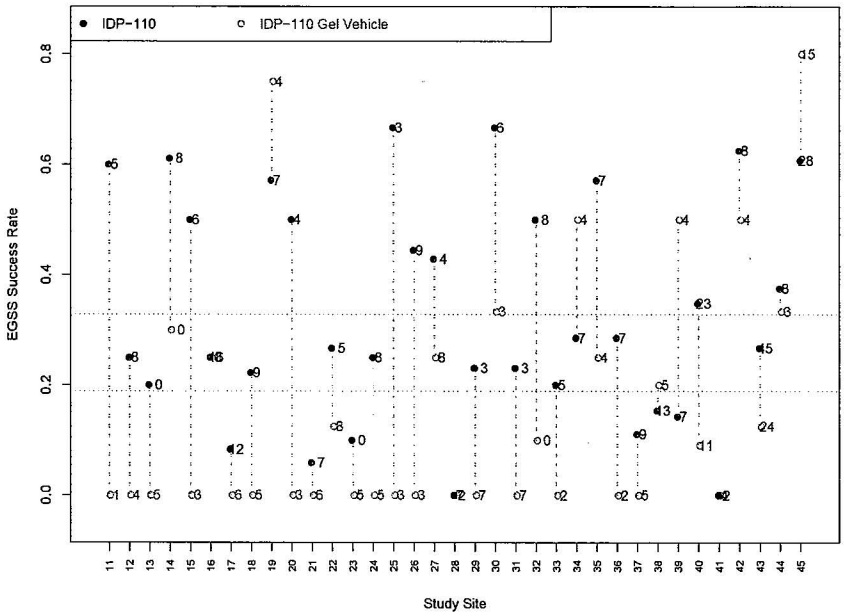
3.1.7 Efficacy Results by Center

Study 012 enrolled subjects from a total of 35 investigative sites, 33 from the US, 1 from Canada, and 1 from Central America (Belize). Study 017 enrolled subjects from 33 investigative sites, all from the US. The maximum number of enrollment by one site was 162 (11.4% of the total number of subjects) and 92 (6.5%) in Studies 012 and 017, respectively. In both studies, investigative sites were pooled into 28 pooled centers.

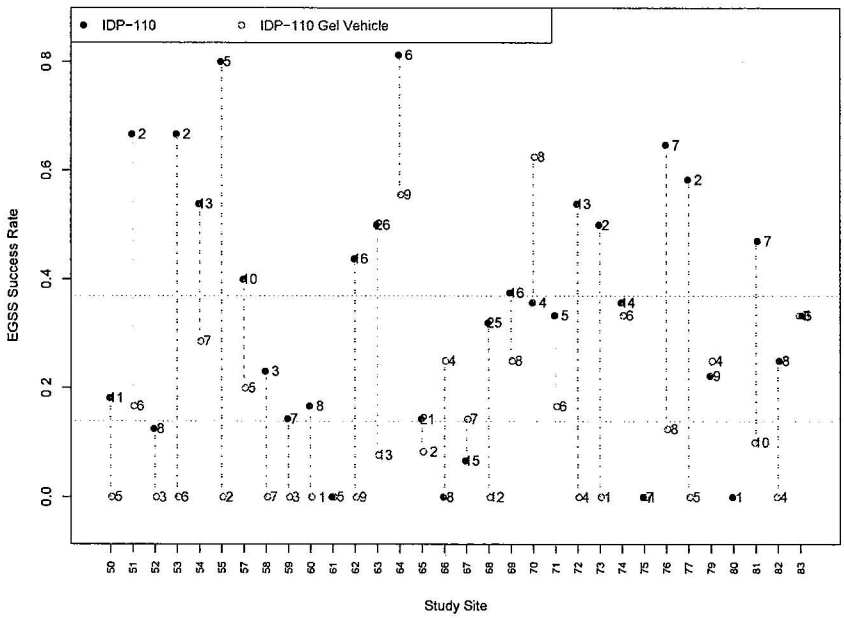
Figure 3 presents the success rate based on EGSS and number of subjects enrolled by each investigative site in the IDP-110 and vehicle arms. The treatment effect appeared to be relatively consistent across the pooled sites, and therefore the results do not seem to be driven by extreme sites.

Figure 4 and 5 present the mean absolute change in inflammatory and non-inflammatory lesion counts at Week 12 from baseline by site in the IDP-110 and vehicle arms. The treatment effect on both lesion types appeared to be consistent across the investigative sites. The results do not seem to be driven by extreme sites.

Figure 3: EGSS by Investigative Site

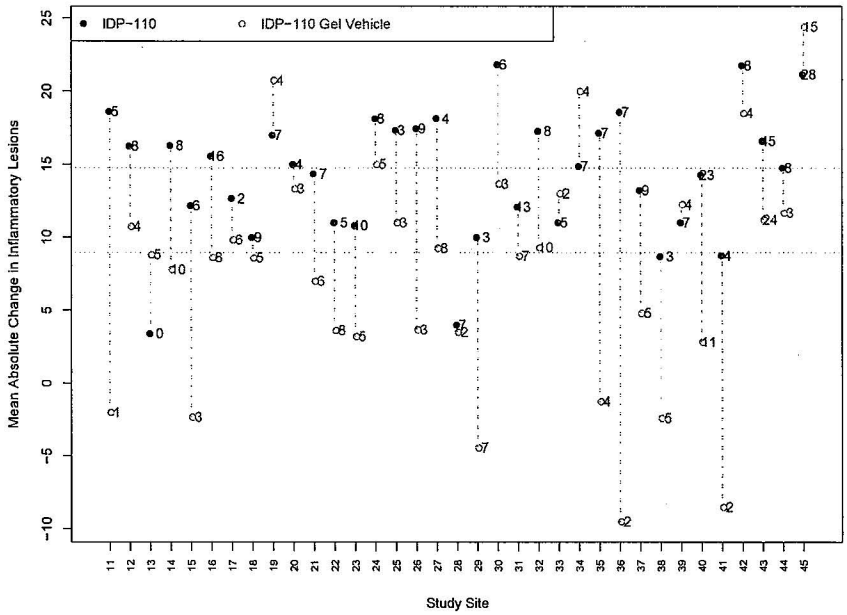


(a) Study 012

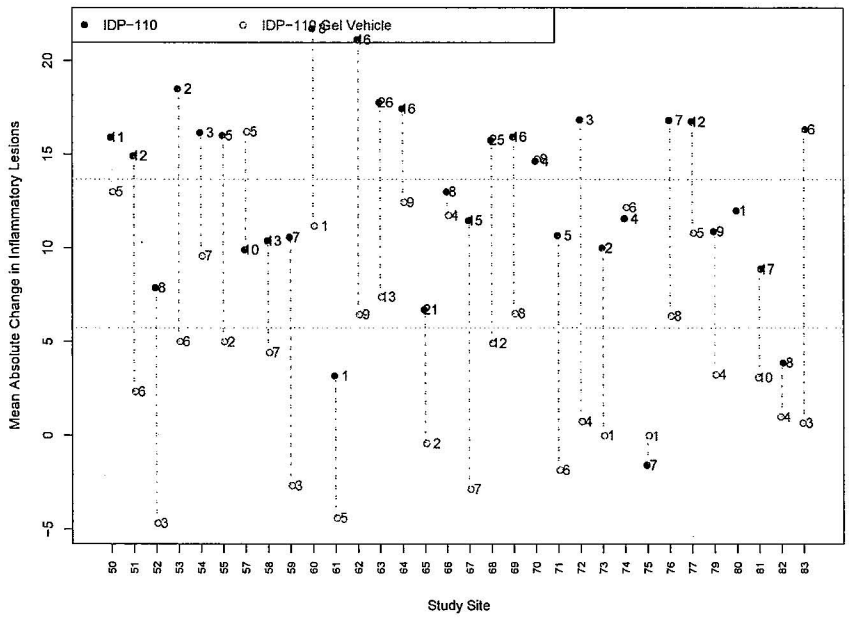


(b) Study 017

Figure 4: Mean Absolute Change in Inflammatory Lesion Count from Baseline by Investigative Sites

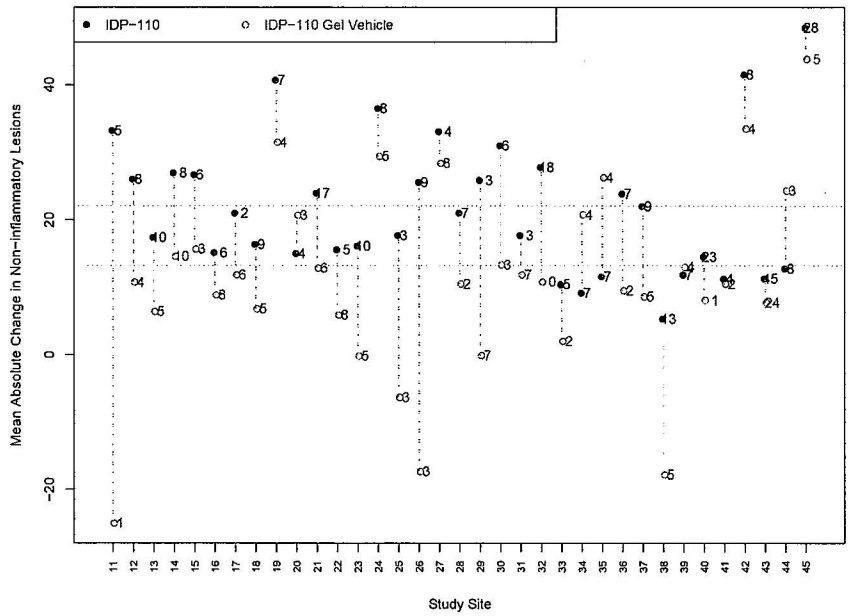


(a) Inflammatory: Study 012

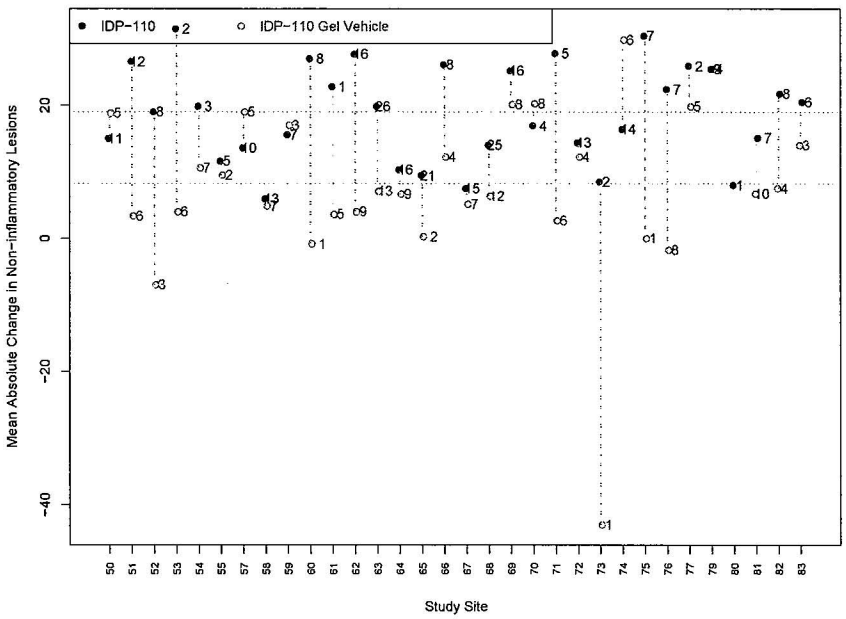


(b) Inflammatory: Study 017

Figure 5: Mean Absolute Change in Non-Inflammatory Lesion Count from Baseline by Investigative Sites



(a) Non-inflammatory: Study 012



(b) Non-inflammatory: Study 017

3.2 Evaluation of Safety

Subjects who had documented use of study medication and at least one post-Baseline evaluation were included in the safety evaluation. There were 1335 and 1352 subjects in Studies 012 and 017, respectively that were evaluated for safety. This section includes the extent of drug exposure and adverse events.

3.2.1 Extent of Exposure

The duration of treatment was defined as (date of last application date)-(date of baseline visit)+1. Most subjects in all four arms used the treatment for 84 days (12 weeks). In both studies and all treatment arms, the median treatment duration was 84 days. In Study 012, the mean treatment duration was 82.9 (range 9 - 116 days) in the IDP-110 arm, 82.2 (2 - 119 days) and 81.8 (4 - 135 days) in the clindamycin and BPO arms, and 80.8 (9 - 120 days) in the vehicle arm. The mean treatment duration was very similar across treatment arms in Study 017: 82.8 (range 1 - 102 days) in the IDP-110 arm, 84.0 (6 - 109 days) and 82.9 (1 - 115 days) in the clindamycin and BPO arms, and 81.4 (11 - 99 days) in the vehicle arm.

3.2.2 Adverse Events

A total of 339 (25.4%) and 301 (22.3%) subjects in Studies 012 and 017, respectively reported at least one adverse event. The proportion of subjects who experienced such AEs was highest in the BPO arm (28.5%), followed by IDP-110 (27.5%), vehicle (26.6%) and clindamycin (19.7%) in Study 012. In Study 017, the proportion of subjects who experienced at least one AE was highest in IDP-110 arm (24.8%), followed by clindamycin (22.3%), vehicle (21.6%) and BPO (20.5%). Table 14 presents AE rates by system organ classes (SOC) that at least 1% of the subjects per treatment arm experienced.

The most common AEs in the infections and infestations class were nasopharyngitis and upper respiratory tract infection in both studies. The proportion of subjects who experienced nasopharyngitis was highest in BPO subjects (5.3%) in Study 012 and in IDP-110 (3.4%) in Study 017. Upper respiratory tract infection was highest in the IDP-110 arm (4.7%) in Study 012 and in BPO (6.5%) in Study 017. Headache was the most common AE among the nervous system disorders. The sponsor defined serious adverse events (SAE) as any event that resulted in death, a life-threatening event, required hospitalization or prolonged an existing hospitalization, caused a persistent or significant disability/incapacity, resulted in congenital anomaly or birth defect, or was considered a medically important event. In Study 012 four SAEs were reported. In the IDP-110 arm, the reported SAE was uterine leiomyoma which was considered by the sponsor as not related to the study drug. Possible congestive heart failure, gun shot wound and breast cancer were reported as SAE in the clindamycin and BPO arms. In Study 017, 6 SAEs were reported. Depression and oppositinal defiant disorder were reported in the IDP-110 arm,

Table 14: AEs by System Organ Class in at Least 1% of Subjects per Treatment Arm

	Study 012			
SOC	IDP-110 n=386	Clindamycin n=385	BPO n=376	Vehicle n=188
Infections and infestations	56 (15.0%)	41 (10.6%)	62 (16.5%)	29 (15.4%)
Nervous system disorders	12 (3.1%)	11 (2.9%)	10 (2.7%)	5 (2.7%)
Respiratory, thoracic and mediastinal disorders	8 (2.1%)	8 (2.1%)	12 (3.2%)	3 (1.6%)
Gastroinetestinal disorders	6 (1.6%)	8 (2.1%)	5 (1.3%)	7 (3.7%)
Injury, poisoning and procedural complications	12 (3.1%)	7 (1.8%)	11 (2.9%)	6 (3.2%)
Psychiatric disorders	5 (1.3%)	4 (1.0%)	3 (0.8%)	0 (0.0%)
Skin and subcutaneous tissue disorders	3 (0.8%)	3 (0.8%)	9 (2.4%)	3 (1.6%)
General disorders and administration site conditions	2 (0.5%)	3 (0.8%)	5 (1.3%)	2 (1.1%)
Musculoskeleta and connective tissue disorders	4 (1.0%)	2 (0.5%)	4 (1.1%)	2 (1.1%)

	Study 017			
SOC	IDP-110 n=387	Clindamycin n=385	BPO n=385	Vehicle n=185
Infections and infestations	54 (14.0%)	52 (13.5%)	54 (14.0%)	18 (9.7%)
Respiratory, thoracic and mediastinal disorders	17 (4.4%)	14 (3.6%)	5 (1.3%)	10 (5.4%)
Gastroinetestinal disorders	6 (1.6%)	7 (1.8%)	7 (1.8%)	1 (0.5%)
Injury, poisoning and procedural complications	5 (1.3%)	7 (1.8%)	5 (1.3%)	4 (2.2%)
Nervous system disorders	16 (4.1%)	5 (1.3%)	6 (1.6%)	4 (2.2%)
General disorders and administration site conditions	2 (0.5%)	4 (1.0%)	3 (0.8%)	3 (1.6%)
Skin and subcutaneous tissue disorders	4 (1.0%)	2 (0.5%)	5 (1.3%)	4 (2.2%)
Surgical and medical procedures	1 (0.3%)	0 (0.0%)	4 (1.0%)	0 (0.0%)

Source: Study Report DPSI-06-22-2006-012, pg. 301-308; and Study Report DPSI-06-22-2006-017, pg. 300-306.

which were both considered as unrelated or unlikely related to the study drug by the sponsor. Other SAEs were moderate events of appendicitis and cellulitis, small intestinal obstruction and gallstones in the clindamycin and BPO arms, which the sponsor considered as unrelated or unlikely related to the study drug. No deaths were reported in either study.

4 Findings in Special/Subgroup Populations

4.1 Gender, Race, and Age

In this section, the efficacy of IDP-110 was evaluated by subgroup based on the EGSS. Table 15 presents the EGSS success rates by gender. The success rate in the IDP-110 arm was highest

in both females and males. In Study 012, the success rate in females was higher than in males in the active treatment arms: IDP-110, clindamycin and BPO arms. In Study 017, females had higher success rates in IDP-110 and clindamycin arms. The success rates in the BPO arm were similar in both genders.

Table 15: Number (%) of Successes on EGSS by Gender

		Study 012			
Gender		IDP-110 n=399	Clindamycin n=408	BPO n=406	Vehicle n=201
Female	Total	215	215	239	94
	Success (%)	79 (36.7%)	56 (26.0%)	61 (25.5%)	16 (17.0%)
Male	Total	184	193	167	107
	Success (%)	52 (28.3%)	44 (22.8%)	35 (21.0%)	22 (20.6%)

		Study 017			
Gender		IDP-110 n=398	Clindamycin n=404	BPO n=403	Vehicle n=194
Female	Total	193	205	216	98
	Success (%)	75 (38.9%)	64 (31.2%)	60 (27.8%)	16 (16.3%)
Male	Total	205	199	187	96
	Success (%)	72 (35.1%)	50 (25.1%)	54 (28.9%)	11 (11.5%)

Source: Reviewer analysis.

Table 16 presents the EGSS success rates by age groups. The 25%, 50%, and 75% quantile of age was approximately 15.2, 16.9, and 21.1, respectively. Age groups were formed based on these quantiles. The success rate did not show a trend across age groups and were relatively consistent across age groups.

Table 16: Number (%) of Successes on EGSS by Age Group

		Study 012			
Age Group		IDP-110 n=399	Clindamycin n=408	BPO n=406	Vehicle n=201
12 - 15	Total	148	132	154	76
	Success (%)	42 (28.4%)	29 (22.0%)	38 (24.7%)	9 (11.8%)
16 - 17	Total	90	112	94	44
	Success (%)	28 (31.1%)	29 (25.9%)	24 (25.5%)	11 (25.0%)
18 - 21	Total	74	73	65	27
	Success (%)	29 (39.2%)	24 (32.9%)	11 (16.9%)	8 (29.6%)
22 -	Total	87	91	93	54
	Success (%)	32 (36.8%)	18 (19.8%)	23 (24.7%)	10 (18.5%)

		Study 017			
Age Group		IDP-110 n=398	Clindamycin n=404	BPO n=403	Vehicle n=194
12 - 15	Total	159	155	186	80
	Success (%)	61 (38.4%)	37 (23.9%)	44 (23.7%)	9 (11.3%)
16 - 17	Total	96	96	88	45
	Success (%)	31 (33.3%)	25 (26.0%)	33 (37.5%)	1 (2.2%)
18 - 21	Total	67	61	52	30
	Success (%)	25 (37.3%)	19 (31.1%)	16 (30.8%)	3 (10.0%)
22 -	Total	76	92	77	39
	Success (%)	30 (39.5%)	33 (35.9%)	21 (27.3%)	14 (35.9%)

Source: Reviewer analysis.

Table 17 presents the EGSS success rates by race. The majority of the subjects were White (See Table 21 in Appendix A.1), in which the success rate of the IDP-110 arm was higher than other arms in both studies. Success rate was highest in the Clindamycin arm in 'Other' subgroup in both studies. In Asians, the success rate was highest in the BPO arm. Asian and 'Other' subjects were only a small proportion of the sample and therefore inference from these subgroups has limited meaning.