Abstract #2665
Presented at the 29th European Academy of Dermatology and Venereology (EADV) Congress
29–31 October 2020, Virtual Meeting

INCB054707, a Janus Kinase 1 Inhibitor, for Patients With Moderate-to-Severe Hidradenitis Suppurativa: Results From Two Phase 2 Studies

Afsaneh Alavi, MD,[1,2] Iltefat Hamzavi, MD,[3] Kurt Brown, MD,[4] Leandro L. Santos, MS,[4] Zhaoyin Zhu, PhD,[4] Michael D. Howell, PhD,[4] Joslyn Kirby, MD, MS, Med[5]

[1]Mayo Clinic, Rochester, MN, USA; [2]York Dermatology and Research Centre, Richmond Hill, ON, Canada; [3]Henry Ford Medical Center, Detroit, MI, USA; [4]Incyte Corporation, Wilmington, DE, USA; [5]Penn State Health Milton S. Hershey Medical Center, Hershey, PA, USA

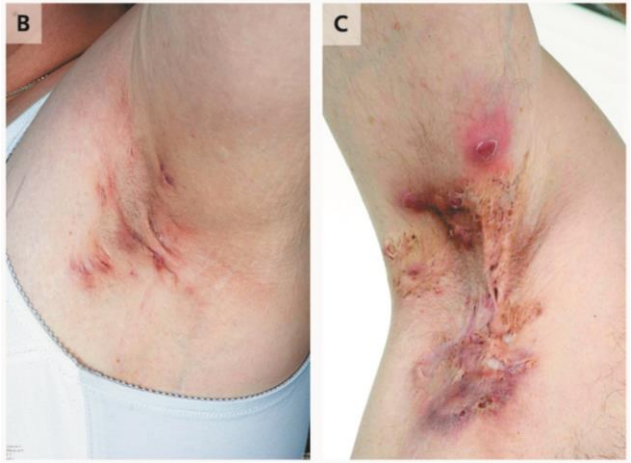
Speaker Disclosures

- Dr Alavi has received honoraria as a consultant, speaker, or advisory board participant from AbbVie, Actelion, Bausch, Celgene, Galderma, GSK, Incyte Corporation, Janssen, LEO Pharma, Novartis, and Sanofi/Genzyme; received grants from AbbVie; and was a research investigator with AbbVie, Aristea, Asana, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Eli Lilly, Genentech, Glenmark, Incyte Corporation, InflaRx, Janssen, Kyowa, Kymera, LEO Pharma, Merck Serono, Novartis, Pfizer, Regeneron, Roche, UCB, Xenon, and Xoma
- INCB054707 is in development for hidradenitis suppurativa and is not currently approved by any regulatory authorities

Background

- Patients with HS experience painful, inflammatory lesions and markedly reduced QoL[1]
- Treatments targeting proinflammatory cytokine signaling may ameliorate HS disease pathology[2]
- INCB054707 is an oral small molecule JAK1 inhibitor with ~52-fold greater selectivity for JAK1 vs JAK2[3]

HS Lesions by Hurley Stage[4]



Stage II Stage III

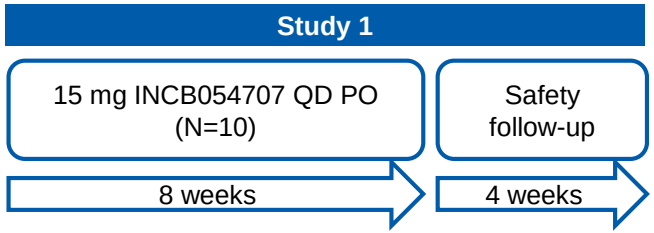
From *N Engl J Med*. Jemec GBE. Hidradenitis suppurativa. 366:158-164, © 2012. Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

HS, hidradenitis suppurativa; JAK, Janus kinase; QoL; quality of life.

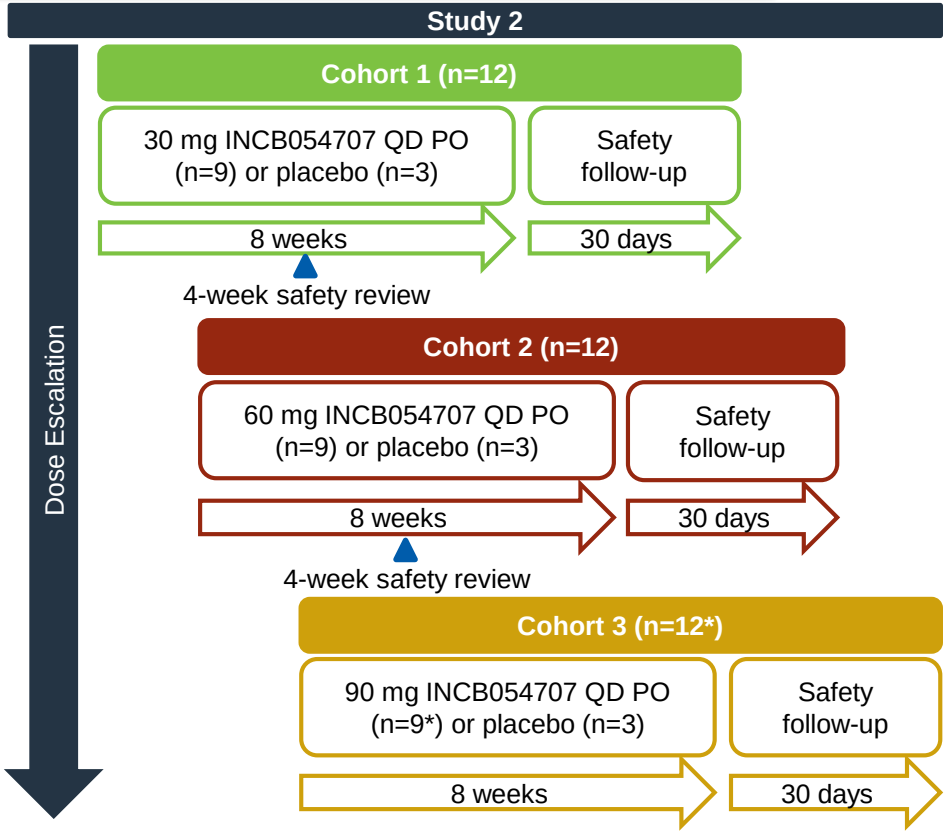
1. MacMahon J, et al. *Patient Relat Outcome Meas*. 2020;11:21-26; 2. Solimani F, et al. *Front Immunol*. 2019;10:2847; 3. Fay B, et al. *Ann Rheum Dis*. 2019;78(suppl 2):OP0280; 4. Jemec GBE. *N Engl J Med*. 2012;366:158-164.

Study Design

- Study 1 (NCT03569371) was a phase 2 open-label, single-arm study



- Study 2 (NCT03607487) was a phase 2 placebo-controlled, dose-escalation study



PO, oral administration; QD, once daily.
* Planned enrollment was 12 patients (9 randomized to 90 mg INCB054707 QD); actual enrollment was 11 patients (8 randomized to 90 mg INCB054707 QD).

Study Endpoints and Eligibility

- **Endpoints**
  - Primary endpoint: safety and tolerability
  - Secondary & exploratory endpoints: HiSCR, AN count, HiSQoL, blood biomarkers

- **Key Inclusion Criteria**
  - Age 18–75 years
  - Moderate-to-severe HS (Hurley stage II/III) of ≥6-months' duration
  - Lesions present in ≥2 anatomic locations
  - Total AN count of ≥3

- **Key Exclusion Criteria**
  - Women who were pregnant or lactating*
  - Presence of >20 draining fistulas at screening and baseline
  - Previous use of JAK inhibitors

AN, abscess and inflammatory nodule; HiSCR, Hidradenitis Suppurativa Clinical Response; HiSQoL, Hidradenitis Suppurativa Quality of Life.
* All other women of childbearing potential were additionally excluded from Study 2.

Patient Demographics and Characteristics

Characteristic	Study 1	Study 2			
	15 mg INCB054707 QD (N=10)	30 mg INCB054707 QD (n=9)	60 mg INCB054707 QD (n=9)	90 mg INCB054707 QD (n=8)	Placebo (n=9)
Age, mean (SD), y	40.7 (14.4)	41.0 (11.5)	42.2 (12.0)	42.8 (14.6)	40.3 (16.7)
Women, n (%)	3 (30.0)	7 (77.8)	8 (88.9)	5 (62.5)	8 (88.9)
White, n (%)	6 (60.0)	7 (77.8)	9 (100.0)	7 (87.5)	8 (88.9)
BMI, mean (SD), kg/m^2	34.2 (9.3)	42.4 (9.5)	41.7 (10.0)	31.8 (6.2)	32.6 (7.8)
Time since first onset of HS, mean (SD), y	16.2 (13.2)	16.8 (12.4)	8.2 (12.5)	13.3 (13.5)	11.1 (13.1)
Hurley stage at baseline, n (%)					
II	7 (70.0)	9 (100.0)	5 (55.6)	7 (87.5)	4 (44.4)
III	3 (30.0)	0	4 (44.4)	1 (12.5)	5 (55.6)
AN count at baseline, mean (SD)	7.3 (4.8)	11.2 (6.7)	16.7 (12.9)	15.9 (15.1)	17.1 (9.6)
Draining fistulas at baseline, mean (SD)	1.6 (2.4)	0.9 (1.1)	3.1 (3.8)	1.8 (3.8)	4.8 (5.4)
Platelet count at baseline, mean (SD), ×10^9/L	318.7 (103.7)	305.3 (50.8)	362.0 (79.5)	260.4 (58.9)	334.2 (90.1)

BMI, body mass index.

TEAEs/TRAEs Occurring in >1 Patient in Any Treatment Group

Parameter	Study 1	Study 2			
	15 mg INCB054707 QD (N=10)	30 mg INCB054707 QD (n=9)	60 mg INCB054707 QD (n=9)	90 mg INCB054707 QD (n=8)	Placebo (n=9)
Any TEAE, n (%)	7 (70.0)	8 (88.9)	6 (66.7)	7 (87.5)	4 (44.4)
Fatigue	0	1 (11.1)	2 (22.2)	3 (37.5)	1 (11.1)
Headache	1 (10.0)	0	2 (22.2)	2 (25.0)	2 (22.2)
Folliculitis	0	2 (22.2)	1 (11.1)	0	1 (11.1)
Nasopharyngitis	0	1 (11.1)	2 (22.2)	0	1 (11.1)
Thrombocytopenia	0	0	0	4 (50.0)	0
Upper respiratory tract infection	3 (30.0)	0	0	1 (12.5)	0
Diarrhea	0	1 (11.1)	0	0	2 (22.2)
Gastroenteritis	0	0	2 (22.2)	0	0
Any TRAE, n (%)	3 (30.0)	4 (44.4)	1 (11.1)	6 (75.0)	2 (22.2)
Headache	1 (10.0)	0	1 (11.1)	2 (25.0)	1 (11.1)
Thrombocytopenia	0	0	0	4 (50.0)	0

TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Safety

In Study 1:

- All TEAEs and TRAEs were mild or moderate
- One patient discontinued due to upper respiratory tract infection and fibromyalgia

In Study 2:

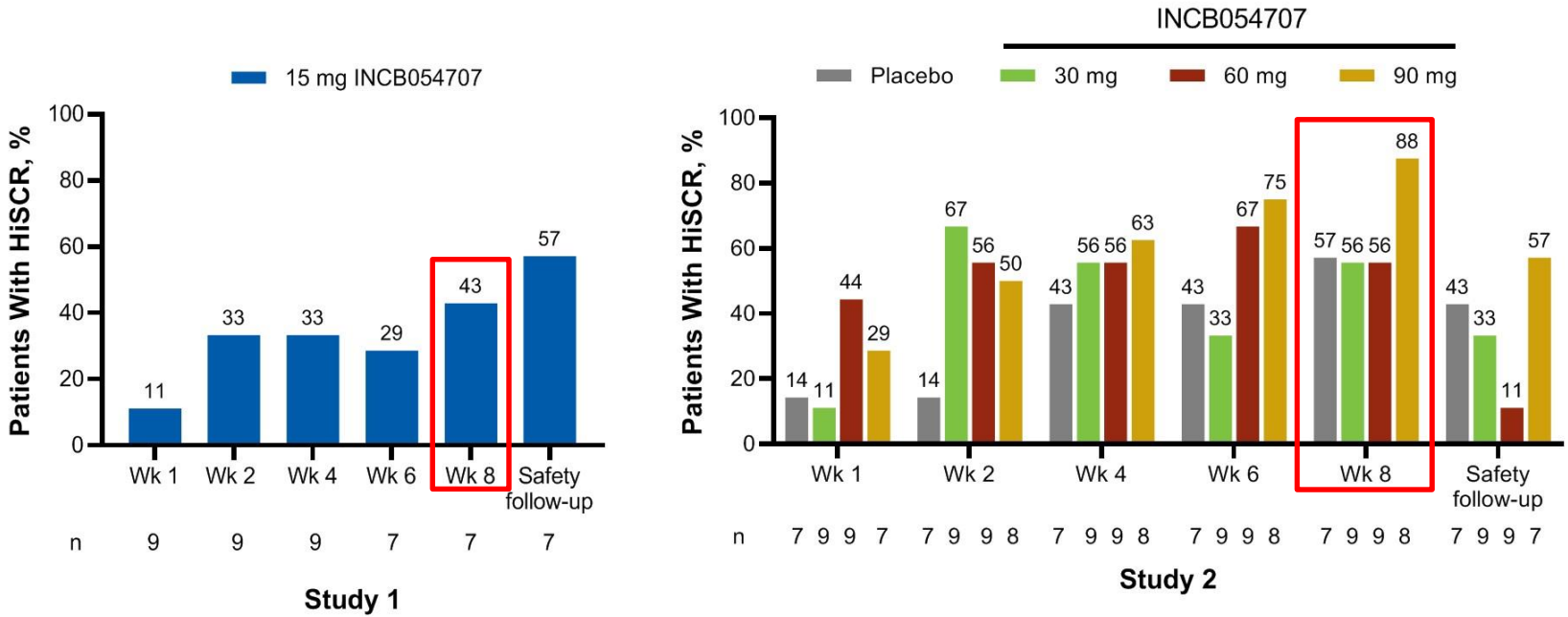
- Four patients (15.4%) treated with INCB054707 (all 90 mg) experienced thrombocytopenia* and had dose interruptions up to 2 weeks
- All platelet counts returned to levels above 100 × 10^9/L, and drug was restarted without sequelae

- There were no serious or fatal TEAEs in either study

*Thrombocytopenia was defined as platelet count <150 × 10^9/L.

HiSCR

Proportion of Patients With HiSCR* at Each Study Visit

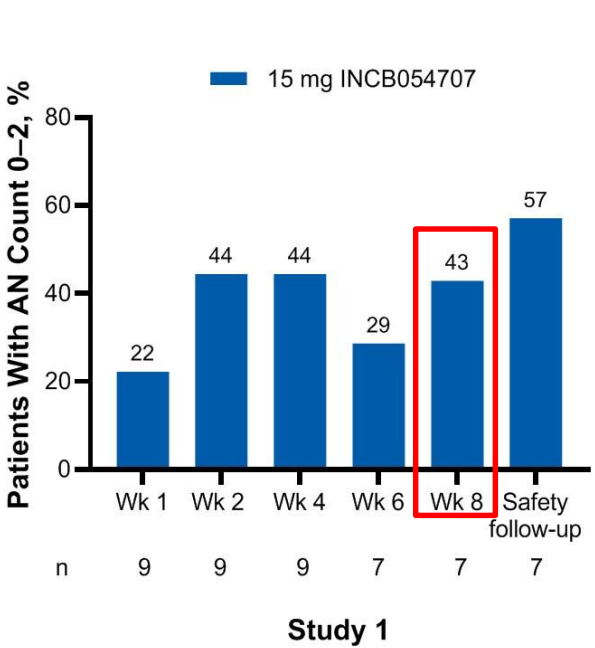


* HiSCR defined as ≥50% reduction in AN count with no increase in either abscess or draining fistula counts relative to baseline.[1]

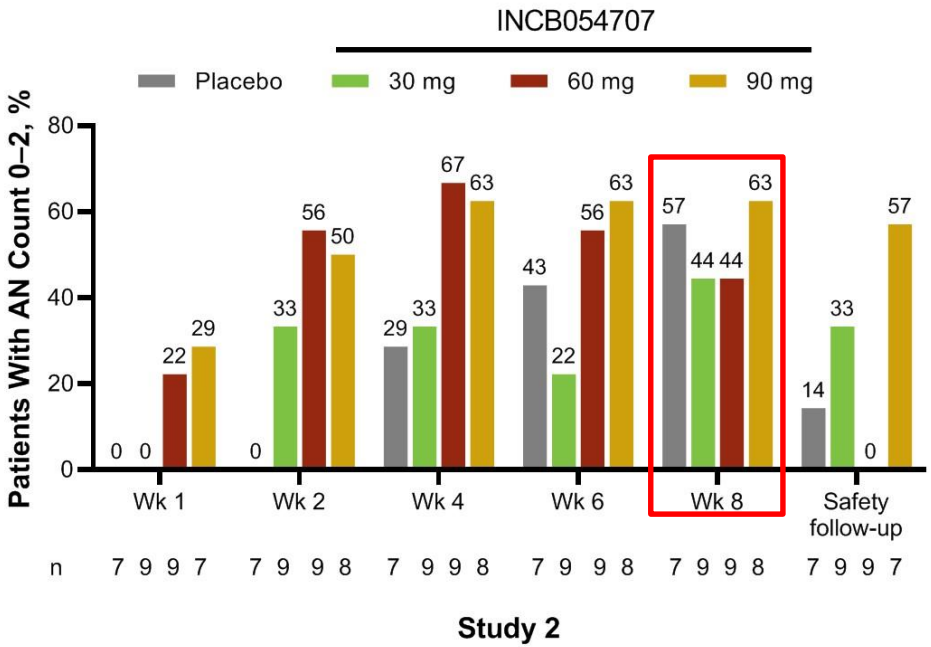
1. Kimball AB, et al. *J Eur Acad Dermatol Venereol*. 2016;30:989-994.

AN Count (0–2)

Proportion of Patients With AN Count 0–2 at Each Study Visit



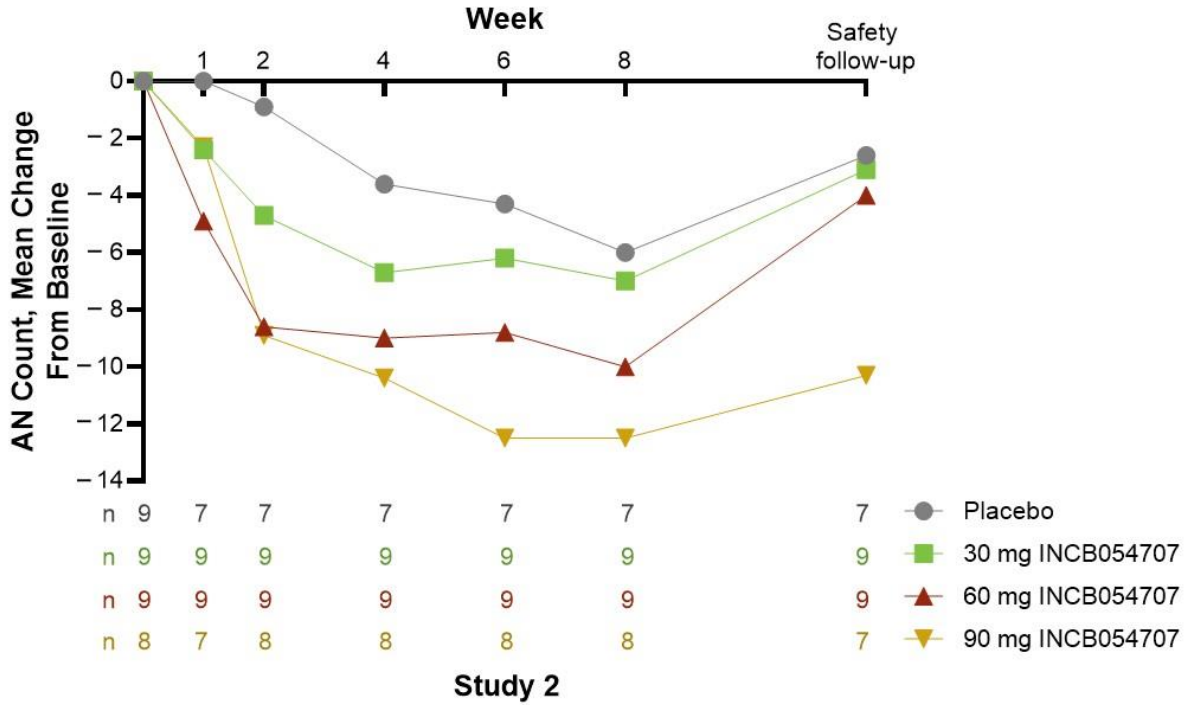
Study 1



Study 2

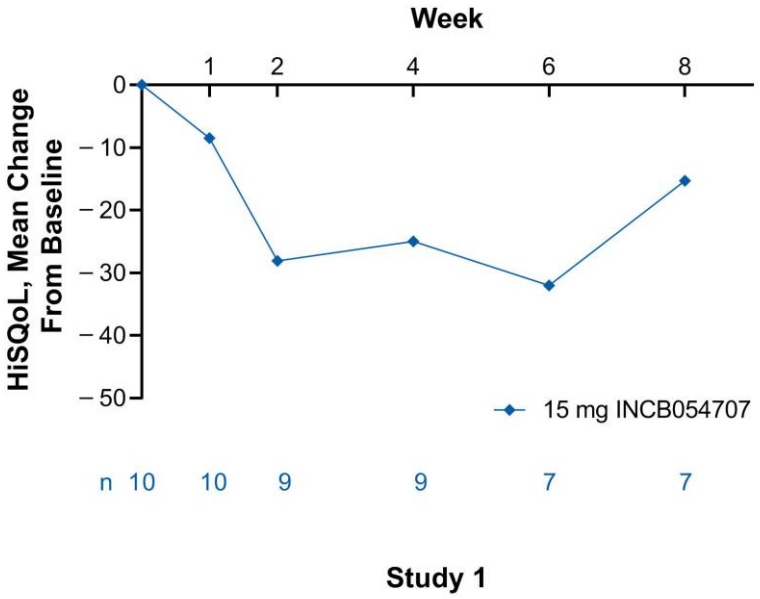
AN Count in Study 2

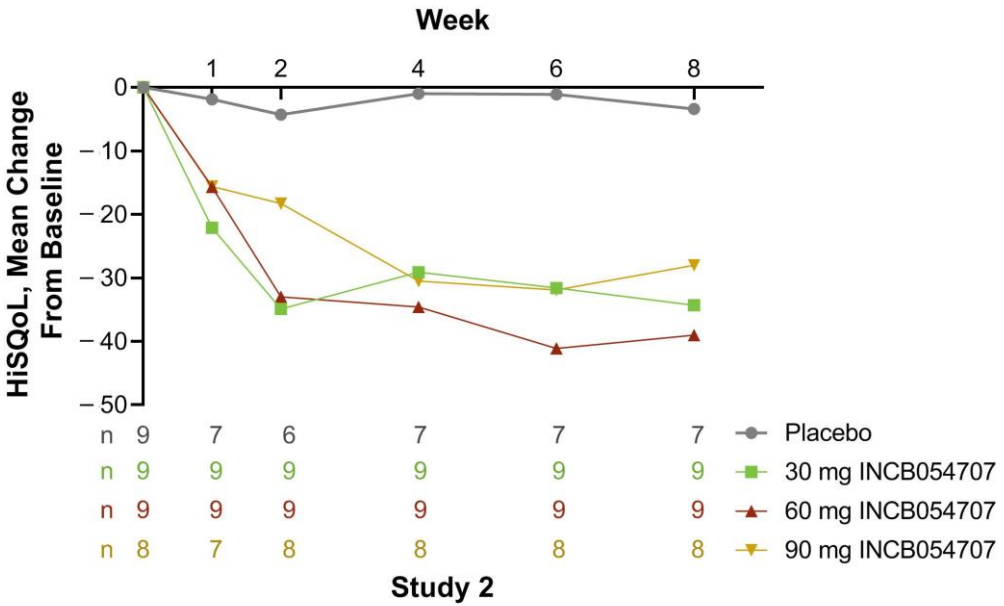
Mean Change From Baseline in AN Count at Each Study Visit



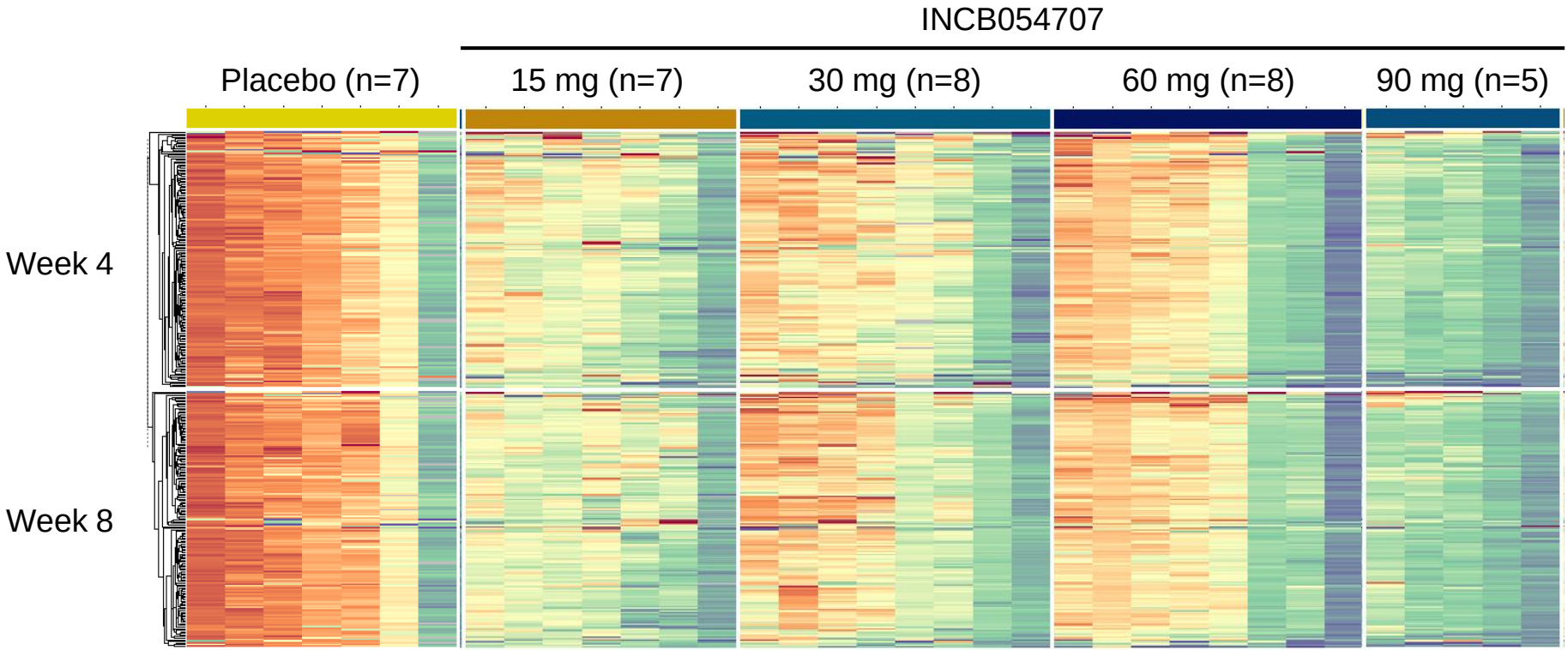
HiSQoL

Mean Change From Baseline in HiSQoL at Each Study Visit





Biomarker Analysis of Inflammatory Mediators



Conclusions

- Orally administered INCB054707 was well tolerated and demonstrated preliminary efficacy in two phase 2 studies in patients with moderate-to-severe HS
  - Only one patient (15 mg INCB054707 QD) discontinued treatment; 4 patients (90 mg INCB054707 QD) had dose interruptions
  - Improvements in AN count were seen as early as Week 1 with INCB054707 and were maintained over the treatment period
- Treatment with INCB054707 was associated with dose-dependent modulation of circulating inflammatory mediators; deeper analysis is ongoing
- Additional clinical studies of JAK1 inhibition for the treatment of HS are warranted