Oral Janus kinase inhibitors PF-06700841 and PF-06651600 provide clinically evident therapeutic effect at 4 and 6 weeks in patients with alopecia areata and greater efficacy over 24 weeks in patients with a shorter duration of their current alopecia episode: Results of a randomized phase 2a trial

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Disclosures

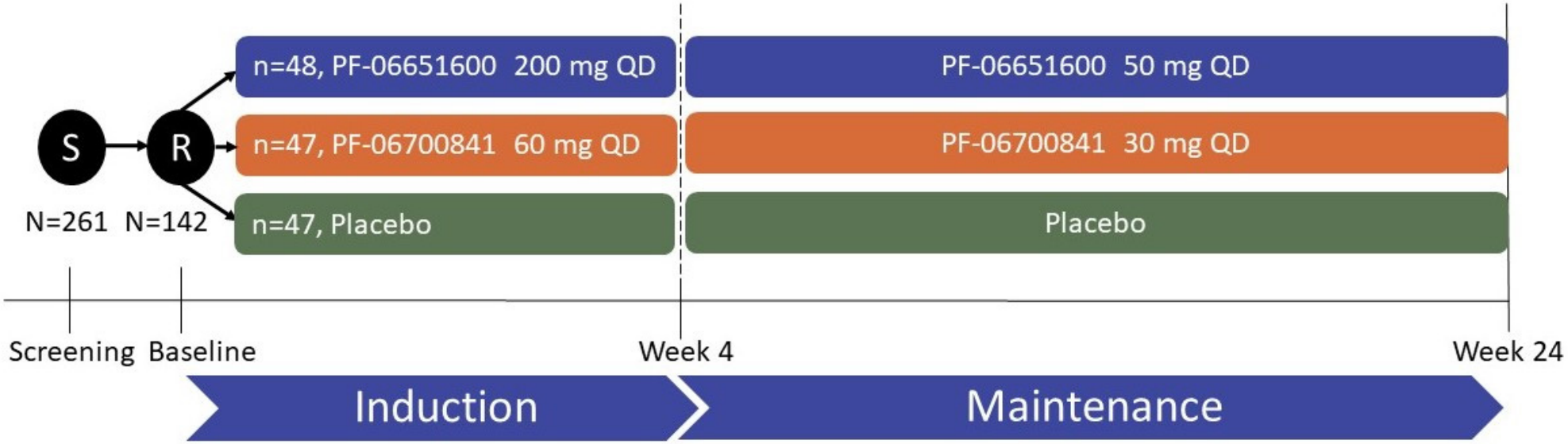
E Peeva	Employee and stockholder of Pfizer
A Banerjee	Employee and stockholder of Pfizer
E Guttman-Yassky	Abbvie, Asana BioSciences, Celgene, Dermavant, Dermira, DS Biopharma, Eli Lilly, Galderma, Glenmark, Innovaderm Research, Janssen, LEO Pharma, Novan, Novartis, Pfizer, Ralexar Therapeutics, Regeneron, Union Therapeutics (grants to institution); and AbbVie, Allergan, Amgen, Asana Biosciences, Celgene, Concert, Dermira, DS Biopharma, Eli Lilly, EMD Serono, Escalier Biosciences, FLX Bio, Galderma, Glenmark, Kyowa, LEO Pharma, Mitsubishi Tanabe, Novartis, Pfizer, Regeneron, Sanofi Aventis, Union Therapeutics (honoraria or consultation fees)
AB Pavel	No conflicts of interests to declare
B Craiglow	Advisory boards, honoraria and consulting fees: Pfizer
R Sinclair	Professional services: Leo Pharma, Amgen, Novartis, Merck & Co., Celgene, Coherus Biosciences, Janssen, Regeneron, MedImmune, GlaxoSmithKline, Cutanea, Samson Clinical, Boehringer Ingelheim, Pfizer, MSD, Oncobiologics, Roche, Eli Lilly and Company, Bayer, and Sun Pharma
C Banfield	Employee and stockholder of Pfizer
M Vincent	Employee and stockholder of Pfizer
L Zhu	Employee and stockholder of Pfizer
B King	Honoraria and/or consultation fees from Aclaris Therapeutics, Concert Pharmaceuticals, Dermavant Sciences, Eli Lilly and Company, and Pfizer

Objectives

- To evaluate the onset of action of PF-06651600, an oral Janus kinase 3 (JAK3) inhibitor, and PF-06700841, an oral tyrosine kinase 2 (TYK2)/JAK1 inhibitor, in moderate to severe alopecia areata
- To evaluate the relationship between the efficacy of PF-06651600 and PF-06700841 over 24 weeks and the duration of the current alopecia areata episode

The primary endpoint was the mean change from baseline in the Severity of Alopecia Tool (SALT) score at Week 24, disclosed at the 27th Congress of the European Academy of Dermatology and Venereology (EADV), 12–16 September 2018, Paris, France.

Study Design



QD, daily; R, randomization; S, screening.

Methods

- Phase 2a, randomized, double-blind, multicenter study with two ongoing extensions (NCT02974868)
- Study population: 18–75-year-old patients with moderate to severe alopecia areata (≥50% scalp hair loss), including patients with alopecia totalis and alopecia universalis
- Analyses for PF-06651600 and PF-06700841 over 24 weeks:
  - Longitudinal analyses of the Severity of Alopecia Tool (SALT) score change from baseline to identify time to the first statistically significant difference from placebo
  - Subgroup analyses of the SALT score change from baseline over time to assess impact of duration of the current alopecia areata episode (<3.5 years compared to ≥3.5 years) on efficacy of PF-06651600 and PF-06700841

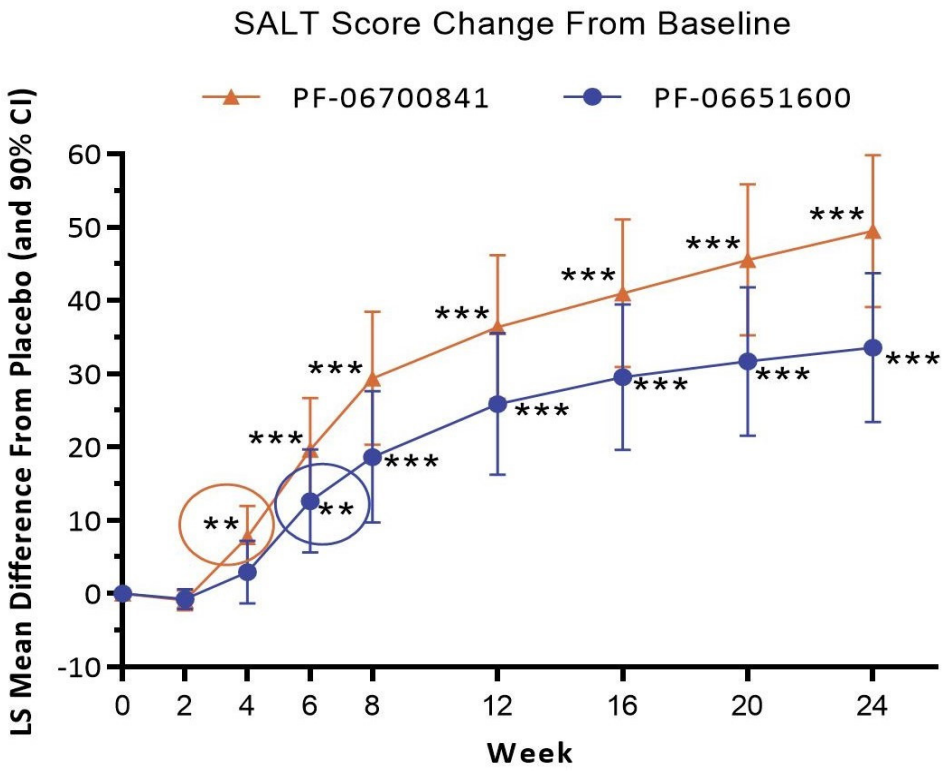
The primary endpoint was the mean change from baseline in the SALT score at Week 24.

Baseline Demographic and Clinical Characteristics

Characteristic	PF-06651600 N=48	PF-06700841 N=47	Placebo N=47
Age, y, mean (SD)	37 (13)	34 (11)	38 (14)
Female, n (%)	37 (77)	32 (68)	29 (62)
Race, n (%)			
White	38 (79)	36 (77)	45 (96)
Black or African American	4 (8)	3 (6)	0
Asian	3 (6)	3 (6)	2 (4)
Other	3 (6)	5 (11)	0
Duration since onset of disease, y, median (range)	6.7 (0.6, 52.3)	8.4 (0.3, 48.5)	5.4 (0.2, 53.4)
Duration of current disease episode, y, median (range)	2.6 (0.3, 7.5)	1.9 (0.2, 7.0)	2.4 (0.2, 29.5)†
SALT Score, mean (SD)	89.4 (15.8)	86.4 (18.1)	88.4 (18.1)
Alopecia totalis, n (%)	20 (42)	22 (47)	20 (43)
Alopecia universalis, n (%)	13 (27)	14 (30)	15 (32)

†Three patients had a long period of waxing and waning hair loss. SALT, Severity of Alopecia Tool; SD, standard deviation.

PF-06700841 and PF-06651600 Provide Clinically Evident Therapeutic Effect at 4 and 6 Weeks, Respectively



Week 4 Mean Difference from Placebo:

PF-06700841: 7.7; *P*=0.002
PF-06651600: 2.9; *P*=0.128

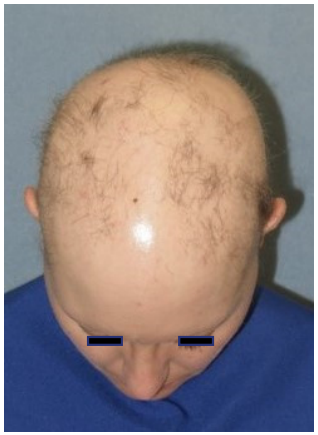
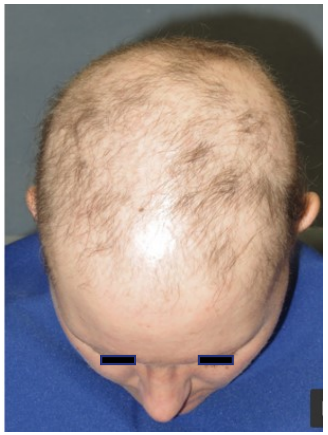
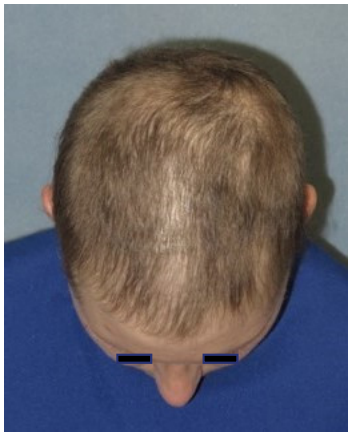
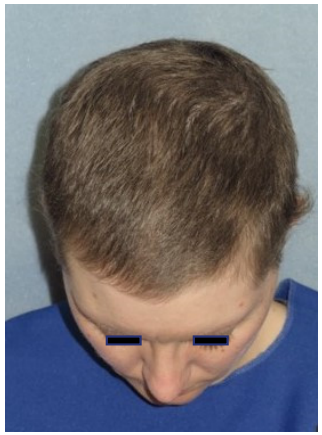
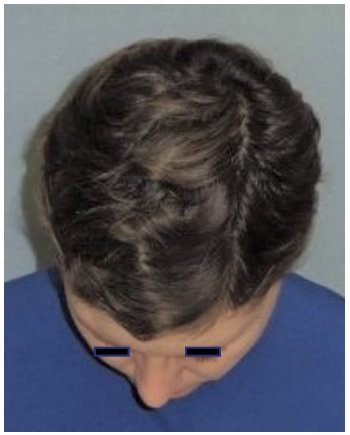
Week 6 Mean Difference from Placebo:

PF-06700841: 19.6; *P*<0.001
PF-06651600: 12.6; *P*=0.002

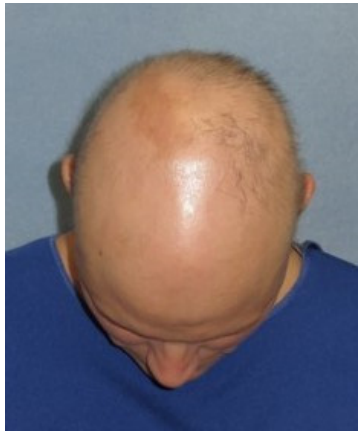
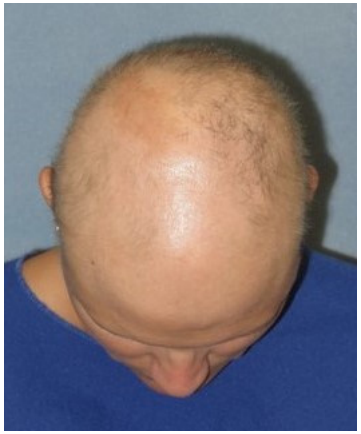
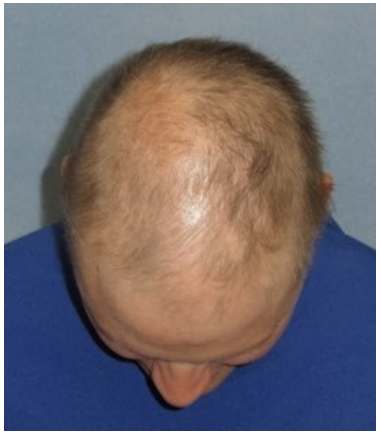
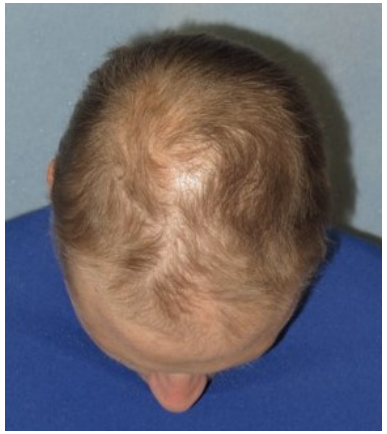
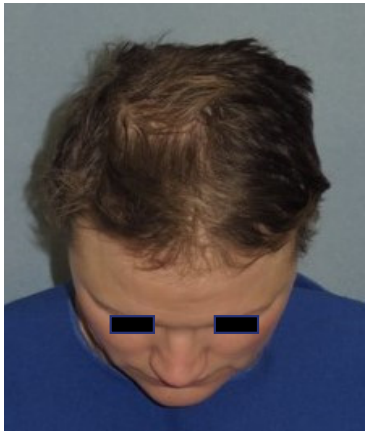
**$P<0.01$, ***$P<0.001$ vs placebo

CI, confidence interval; LS, least squares; SALT, Severity of Alopecia Tool.

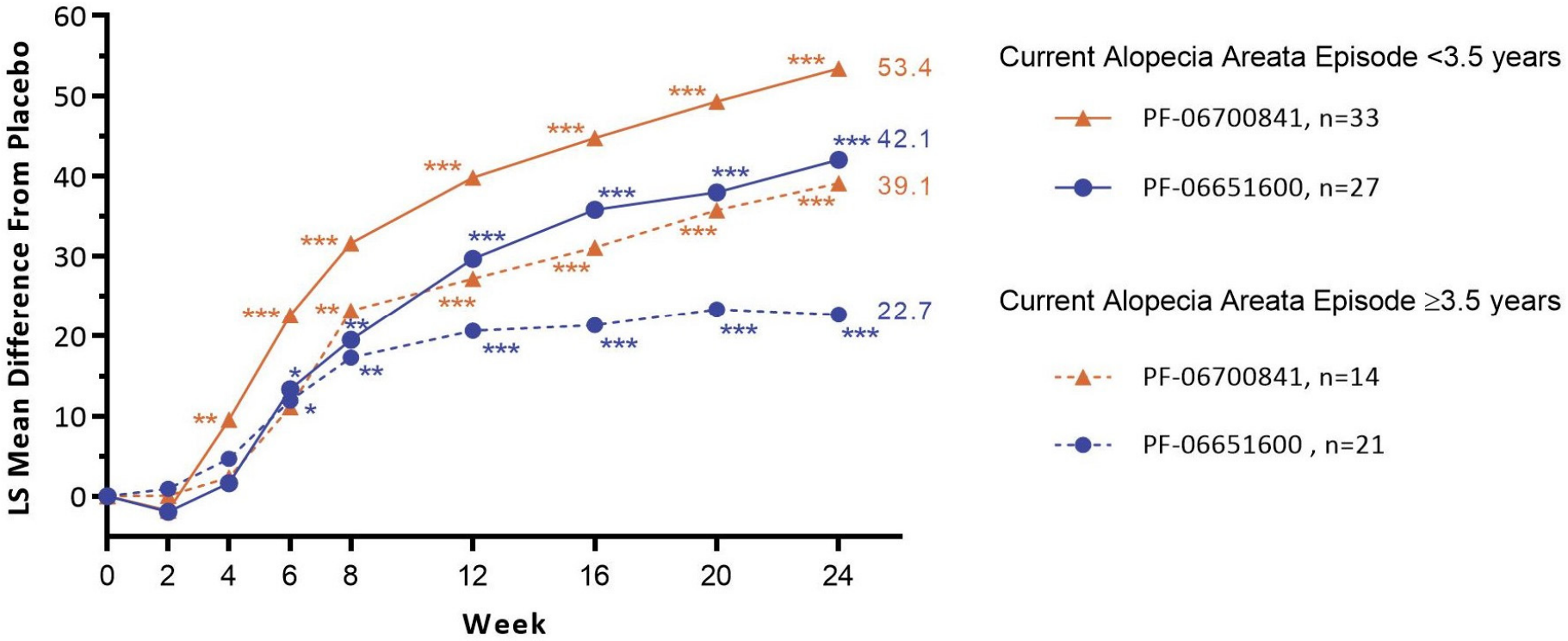
PF-06700841 Responder

Baseline	Week 4	Week 8	Week 12	Week 24
				

PF-06651600 Responder

Baseline	Week 4	Week 8	Week 12	Week 24
				

Difference From Placebo in SALT Score Change From Baseline, Stratified by Episode Duration

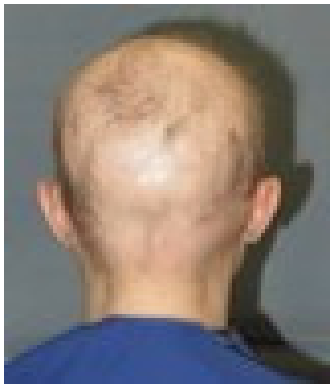


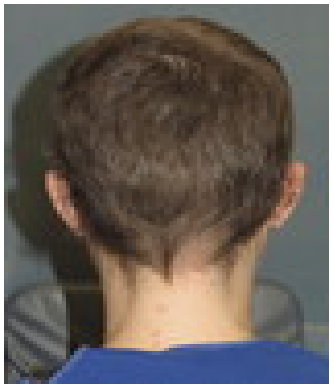
*P<0.05, **P<0.01, ***P<0.001 vs placebo

LS, least-squares; SALT, Severity of Alopecia Tool. n-values are from full analysis set.

PF-06700841 Responders

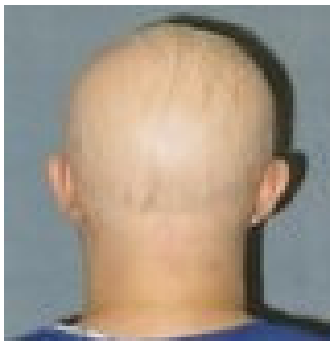
Current Alopecia Areata Episode:
1 year, 10 months

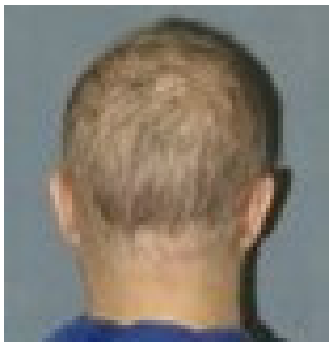


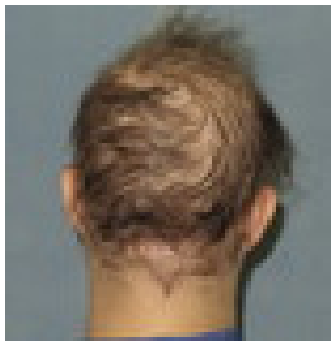


Baseline | Week 12 | Week 24

Current Alopecia Areata Episode:
5 years

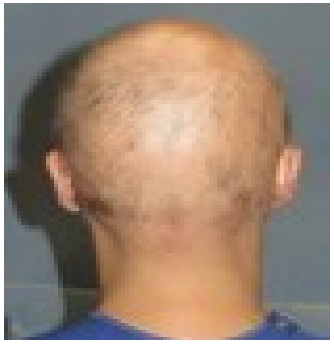


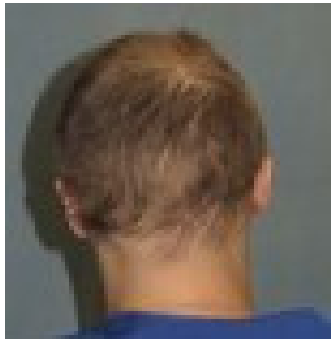


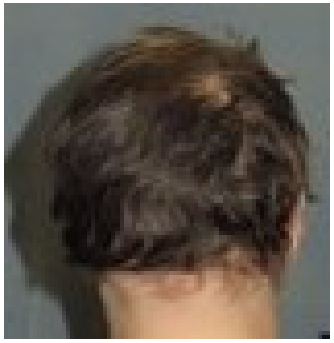


PF-06651600 Responders

Current Alopecia Areata Episode: 9 months

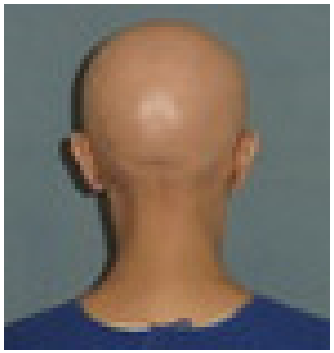


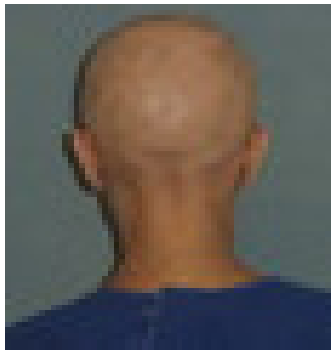


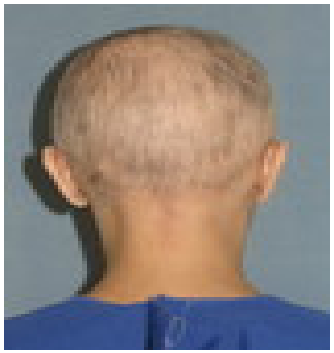


Baseline | Week 12 | Week 24

Current Alopecia Areata Episode: 6 years







Conclusions

- These phase 2 trial data indicate the oral TYK2/JAK1 inhibitor PF-06700841 and the oral JAK3 inhibitor PF-06651600 have an onset of effect at 4 weeks and 6 weeks, respectively
- The 24-week response may be greater in patients with a shorter duration of their current alopecia areata episode

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