#AAD2019

Highlights AEDV

In 77TH AAD Congress

1-5 March 2019

★ Washington ★

Scientific Initiative of:

Sponsored by:

NOVARTIS

#AAD2019

Highlights AEDV

IN 77TH AAD CONGRESS

1-5 MARCH 2019

★ WASHINGTON ★

Psoriasis

Dra. Mar Llamas-Velasco

Scientific Initiative of:

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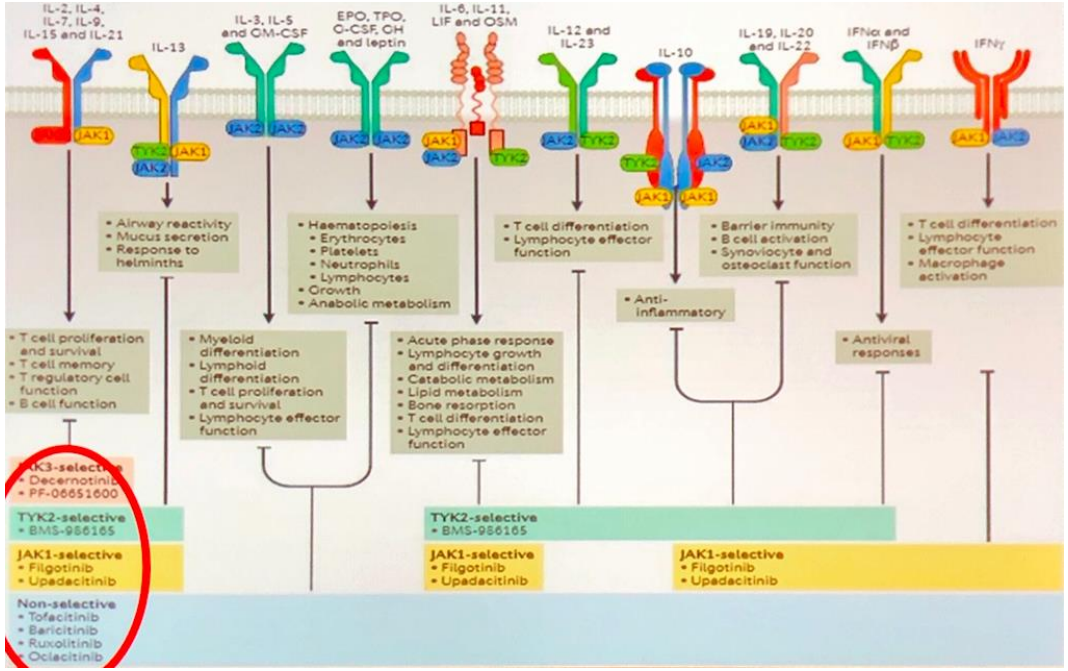
NOVARTIS

SUNDAY 3RD OF MARCH

- New oral treatments
- New biological therapies

NEW ORAL TREATMENTS

- STAT3, JAK/STAK inhibitors
  - Tofacitinib was approved for APs
  - Baricitinib and ruxolitinig for AD.
    - Baricitinib. Papp KA et al. Br J Dermatol 2016; 174: 174: 1266-76.

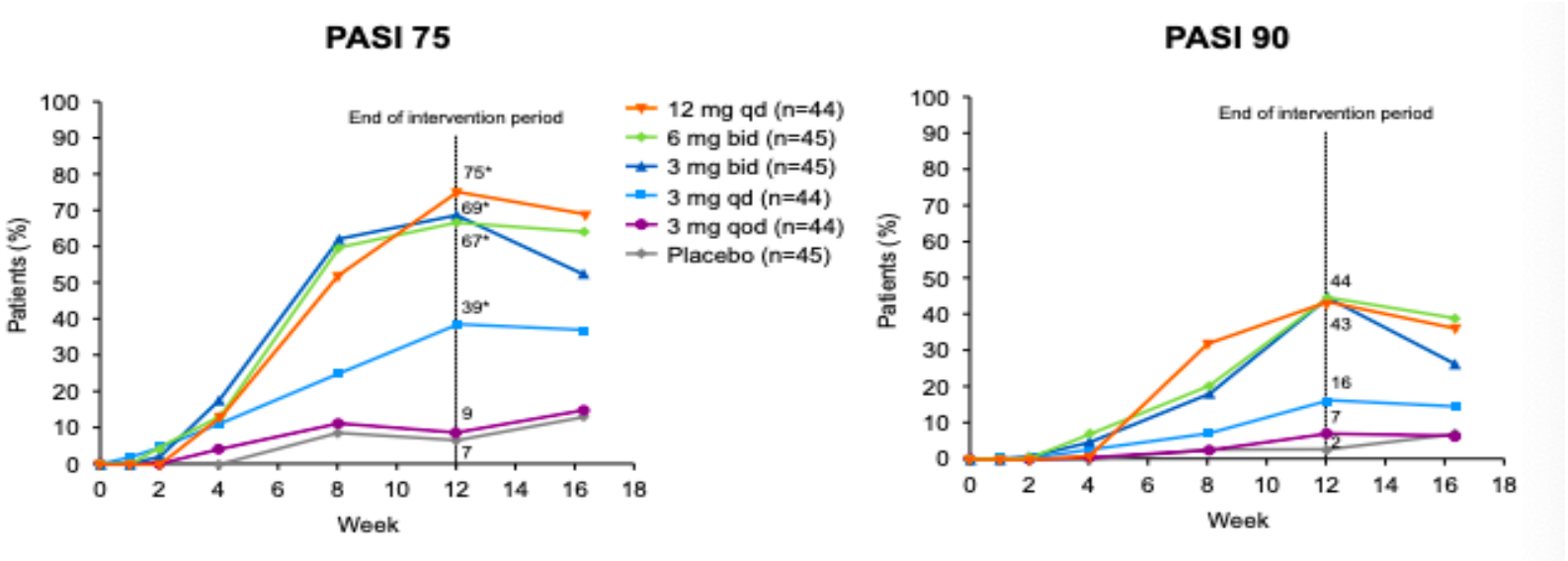


WHAT´S NEW IN PSORIASIS. LEBOWHL

- BMS-986165 treatment reduces the Th17 pathway
- Titration at different doses 3 mg OD/BID, 6 mg BID or 12 mg QD.

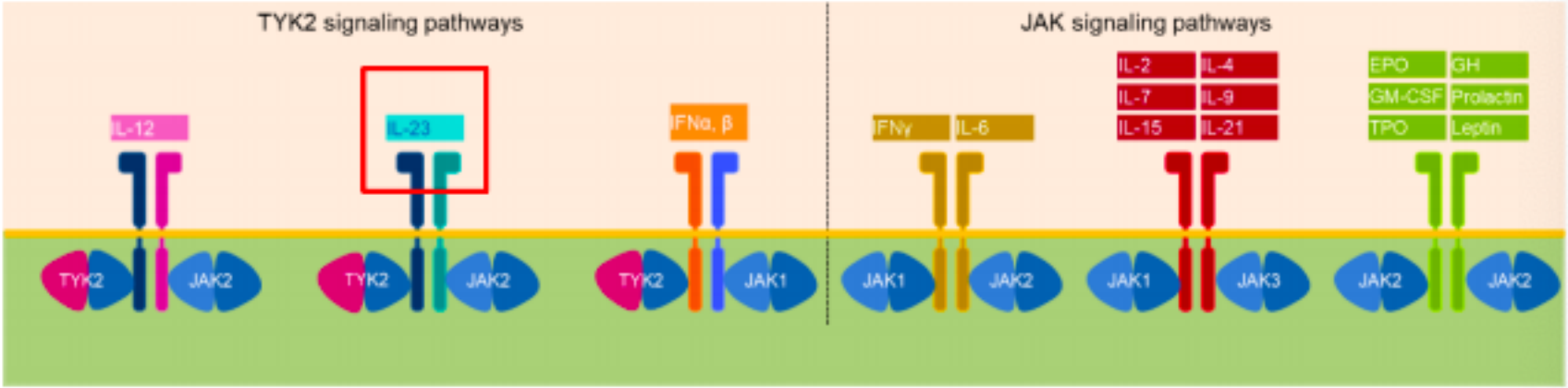
  - Seems not to block biomarkers related to JAK inhibitors. No changes in Hb, NK cell count, Neutrophil count or total cholesterol levels.

  - PHASE 2 trial. PASI response over 12 weeks.



TYK2: S003 Y S009

TYK2 mediates signaling of fewer cytokines compared with JAKs1–3



- BMS-986165 is a molecule that binds selectively to a regulatory domain of TYK2 and changes its conformation such that the kinase activity is inactivated
- This approach has more selectivity than any previous attempt to target the kinase domain of JAKs
- **Is it possible to develop a truly selective TYK2 inhibitor?**

TYK 2

12-week outcomes with oral TYK2 inhibitor in moderate to severe psoriasis

Endpoint	Placebo	3 mg every other day	3 mg daily	3 mg twice a day	6 mg twice a day	12 mg daily
PASI 75	7%	9%	39%	69%	67%	75%
Static Physician's Global Assessment score of 0 or 1	7%	20%	39%	76%	64%	75%
PASI 50	31%	43%	68%	91%	78%	89%
PASI 90	2%	7%	16%	44%	44%	43%
PASI 100	0	2%	0	9%	18%	25%
Dermatology Life Quality Index score of 0 or 1	4%	16%	16%	42%	60%	64%

MDedge News

Note: The randomized, double-blind, placebo-controlled phase 2 study included 267 patients.

Source: N Engl J Med. 2018 Sep 11. doi: 10.1056/NEJMoa1806382

TYK 2

- CLASS EFFECT: ACNE in 2 to 9% of patients. Dose dependent effect.

	Placebo (n=45)	BMS-986165				
		3 mg qod (n=44)	3 mg qd (n=44)	3 mg bid (n=45)	6 mg bid (n=45)	12 mg qd (n=44)
Serious AEs	1 (2)	1 (2)	1 (2)	1 (2)	0	0
AEs	23 (51)	26 (59)	24 (55)	29 (64)	36 (80)	34 (77)
Drug-related AEs	7 (16)	6 (14)	7 (16)	13 (29)	12 (27)	10 (23)
Discontinuations due to AEs	2 (4)	1 (2)	2 (5)	1 (2)	3 (7)	1 (2)
Most frequently reported AEs						
Nasopharyngitis	2 (4)	1 (2)	4 (9)	5 (11)	7 (16)	2 (5)
Headache	2 (4)	4 (9)	4 (9)	3 (7)	3 (7)	2 (5)
Diarrhea	2 (4)	1 (2)	1 (2)	2 (4)	2 (4)	4 (9)
Nausea	2 (4)	4 (9)	0	1 (2)	1 (2)	2 (5)
URTI	0	1 (2)	3 (7)	1 (2)	4 (9)	1 (2)
Acne	0	1 (2)	0	1 (2)	2 (4)	4 (9)

Data are n (%)

- Preliminary but reassuring safety data suggest that TYK2 inhibition with BMS-986165 is selective and well tolerated

PAPP K ET AL. N ENGL J MED 2018.

WHAT ABOUT THE PRIZE?

NEW SYSTEMIC TREATMENTS

- Phase 2 results from XP-23829 a novel fumaric acid ester
  - Extended release FAE
  - Randomized, double-blind placebo-controlled dose-finding efficacy in 33 USA sites.
  - 200 subjets. 1:1:1:1 400 QD; 400 BID, 800 QD or placebo.

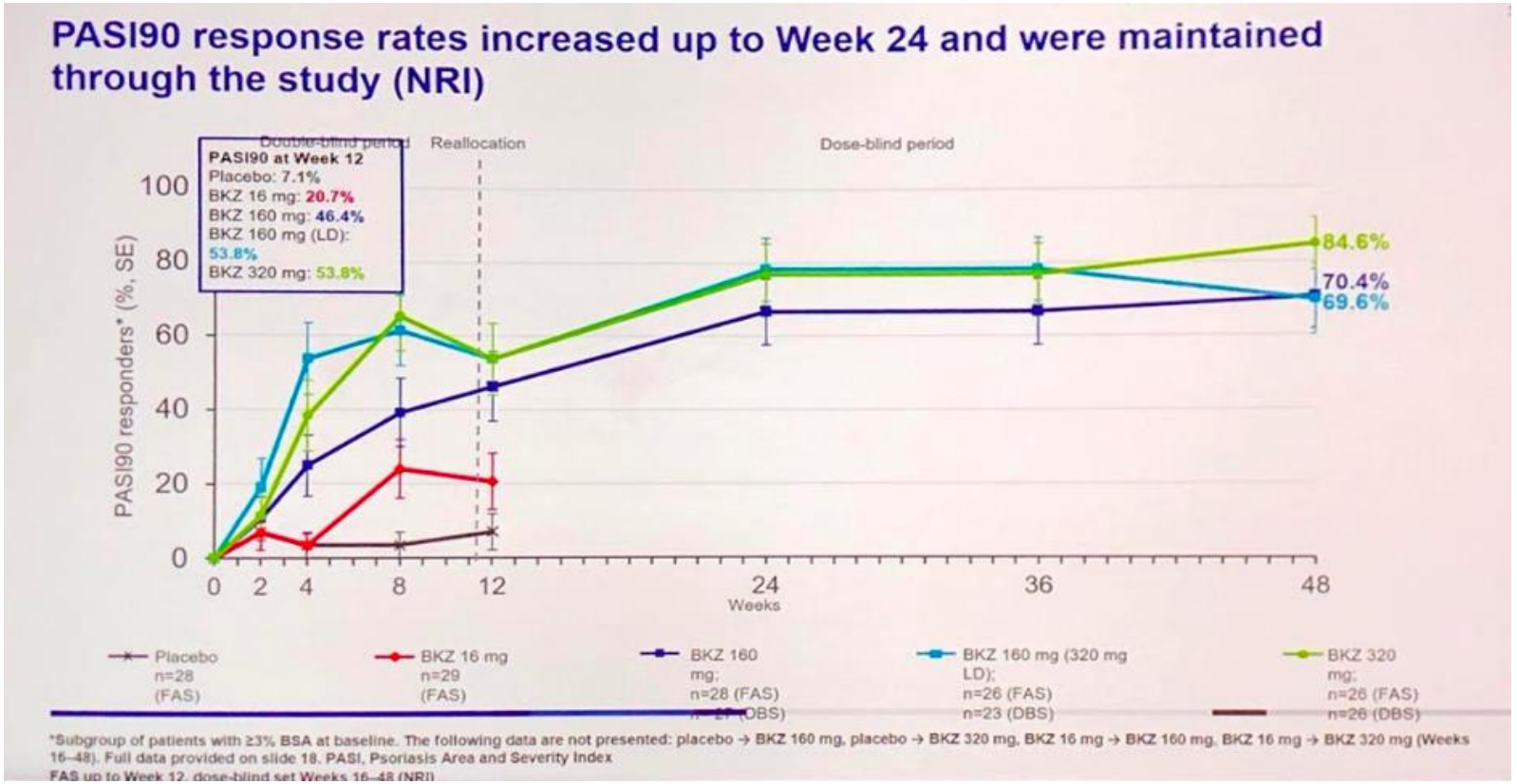
  - Efficacy
    - “Least squares Mean % change: from 25 to 50.7%

  - Safety
    - Diarrhea: Mostly mild.
    - Nausea and abdominal pain more than 10%
    - Flushing in 5.9%. More in the placebo?
    - No lymphopenia.

    - No mean PASI levels, peculiar data on safety, more flushing in placebo.

DUAL INHIBITION IL17A AND IL17F. BIMEKIZUMAB

- Results from the BE ABLE 1, 12 week, placebo controlled phase 2 B trial.
  - PASI 75, 93%; PASI 90 79%; PASI 100 60%.
  - ACR50 response 320 mg. 63.4%. ACR 70 39%.



NEW SYSTEMIC TREATMENTS

- PRUSOL
  - Oral antiretroviral. Finished Phase II. Results pending.

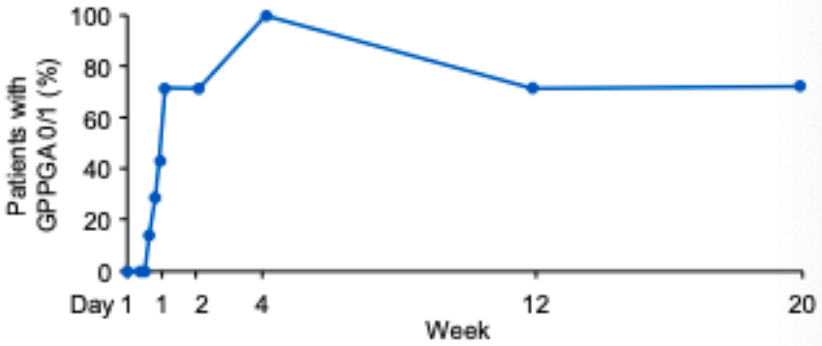
PSORIASIS PUSTULOSA GENERALIZADA

Phase 1 study: Safety and efficacy of BI 655130 for acute generalized pustular psoriasis

Summary of AEs through Week 20

AEs	BI 655130 10 mg/kg (n=7)
Any AE	7 (100)
Severe AE	0
Drug-related AE	
Eosinophilia	4 (57.1)
Vomiting	2 (28.6)
Chills	1 (14.3)
Pain[a]	1 (14.3)
URTI	2 (28.6)
UTI	1 (14.3)
Infusion-related reaction	1 (14.3)
Arthralgia	1 (14.3)
AEs leading to discontinuation	0
Serious drug-related AEs	0

GPPGA total score of 0/1



GPPGA score 0/1 achieved in 5 patients (71.4%) by Week 1, and in all patients by Week 4

- Preliminary evidence in support of safety and efficacy of IL-36R inhibition to treat GPP flares