Nuevas estrategias terapéuticas

1° CONGRESO ARGENTINO de Dermatología Pediátrica de la Sociedad Argentina de Pediatría

28 de Abril de 2017

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Dermatólogo a cargo del Área de Ensayos Clínicos – Psoriahue

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Coordinador del Curso Superior de Dermatología del Colegio de Médicos

Buenos Aires – Argentina

Conflictos de interés

- Honorarios como investigador principal:

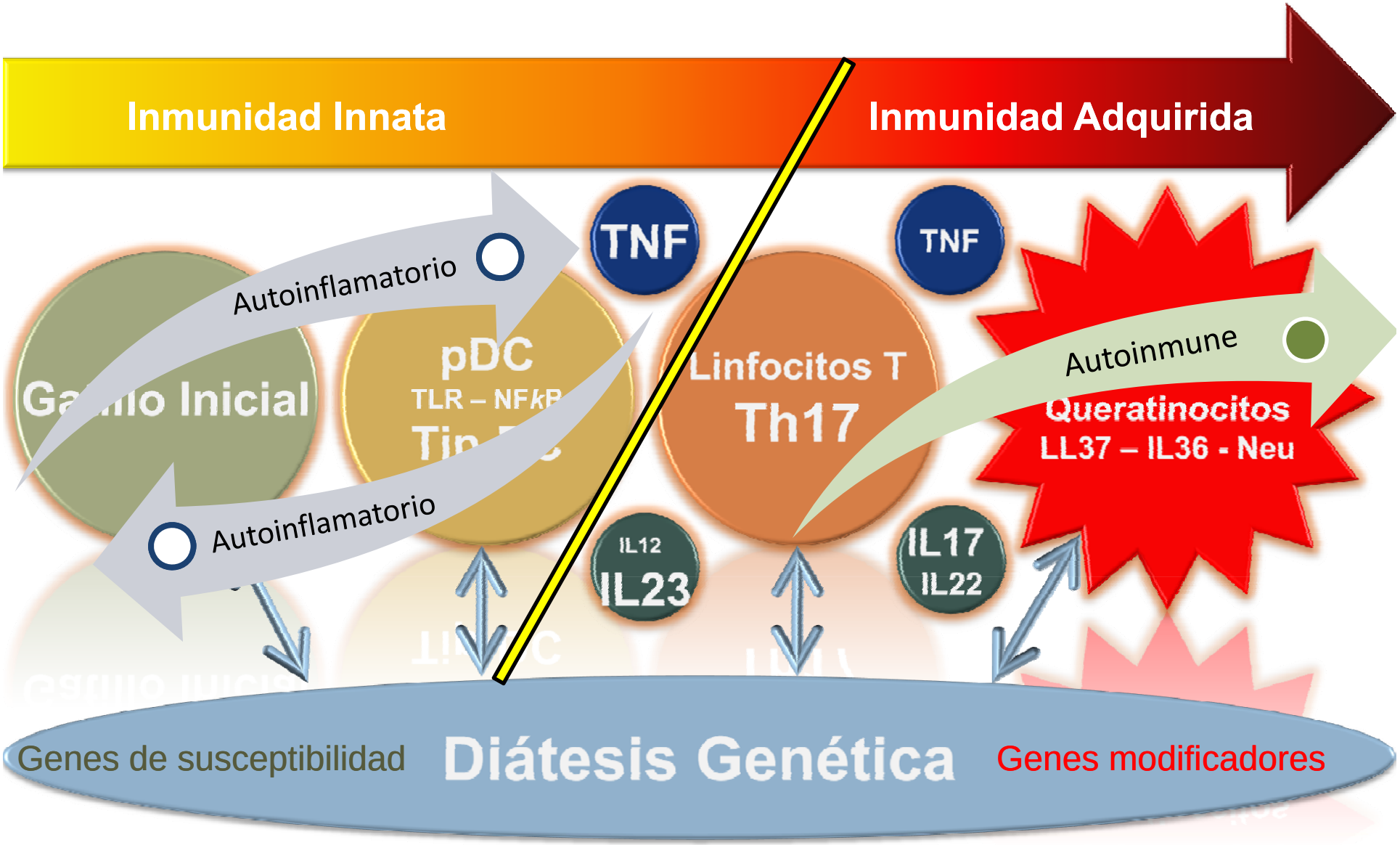
  AbbVie, Eli Lilly, Jannsen Cilag, Novartis.

- Honorarios por conferencias, entrenamientos o asesoramientos eventuales:

  AbbVie, Boehringer Ingelheim, Eli Lilly, Janssen Cilag, Novartis, Pfizer.

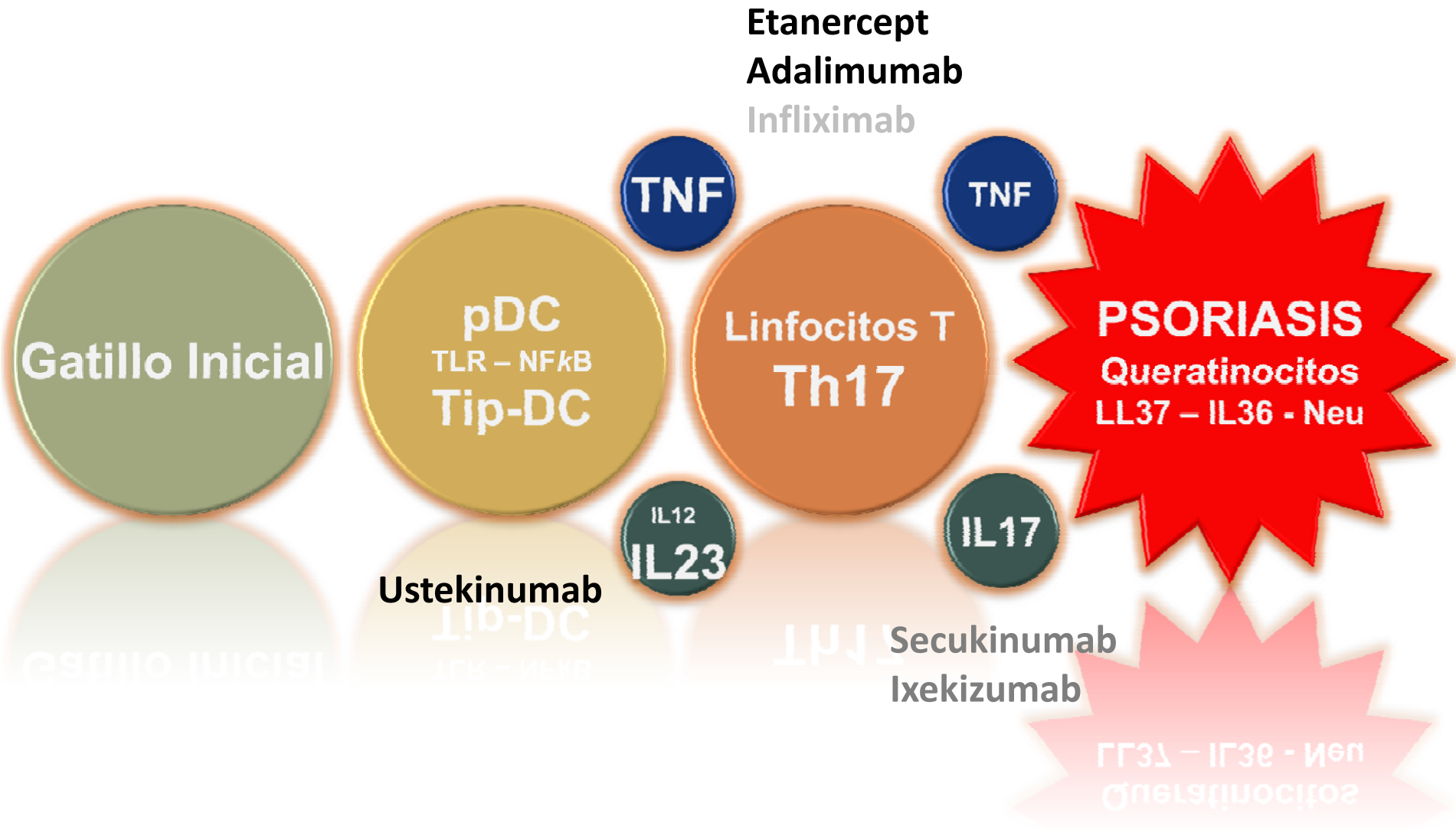

...una Tormenta de Citoquinas

La marcha de la psoriasis

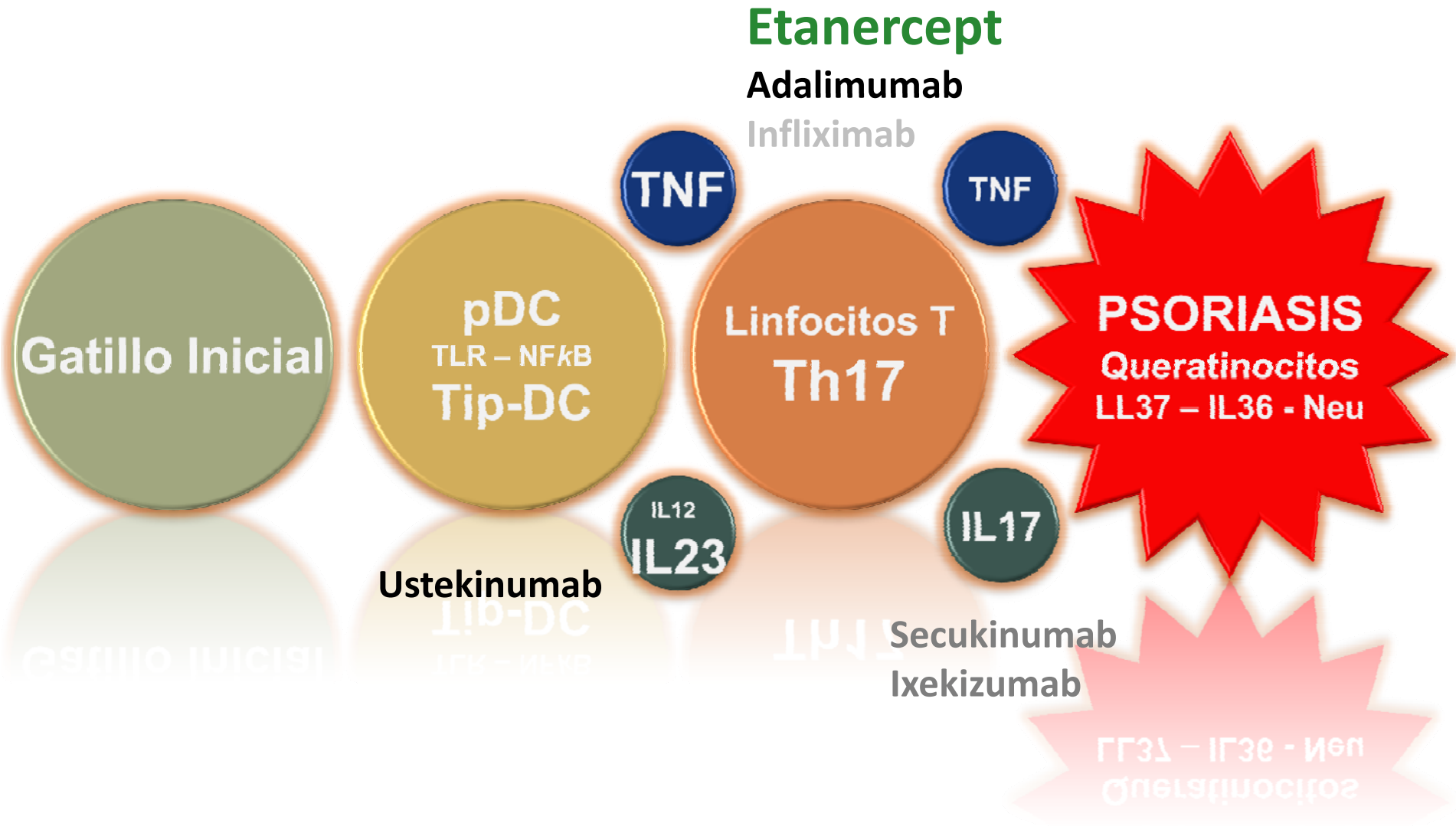



Terapias Biológicas

Blancos y biológicos en la psoriasis



Blancos y biológicos en la psoriasis



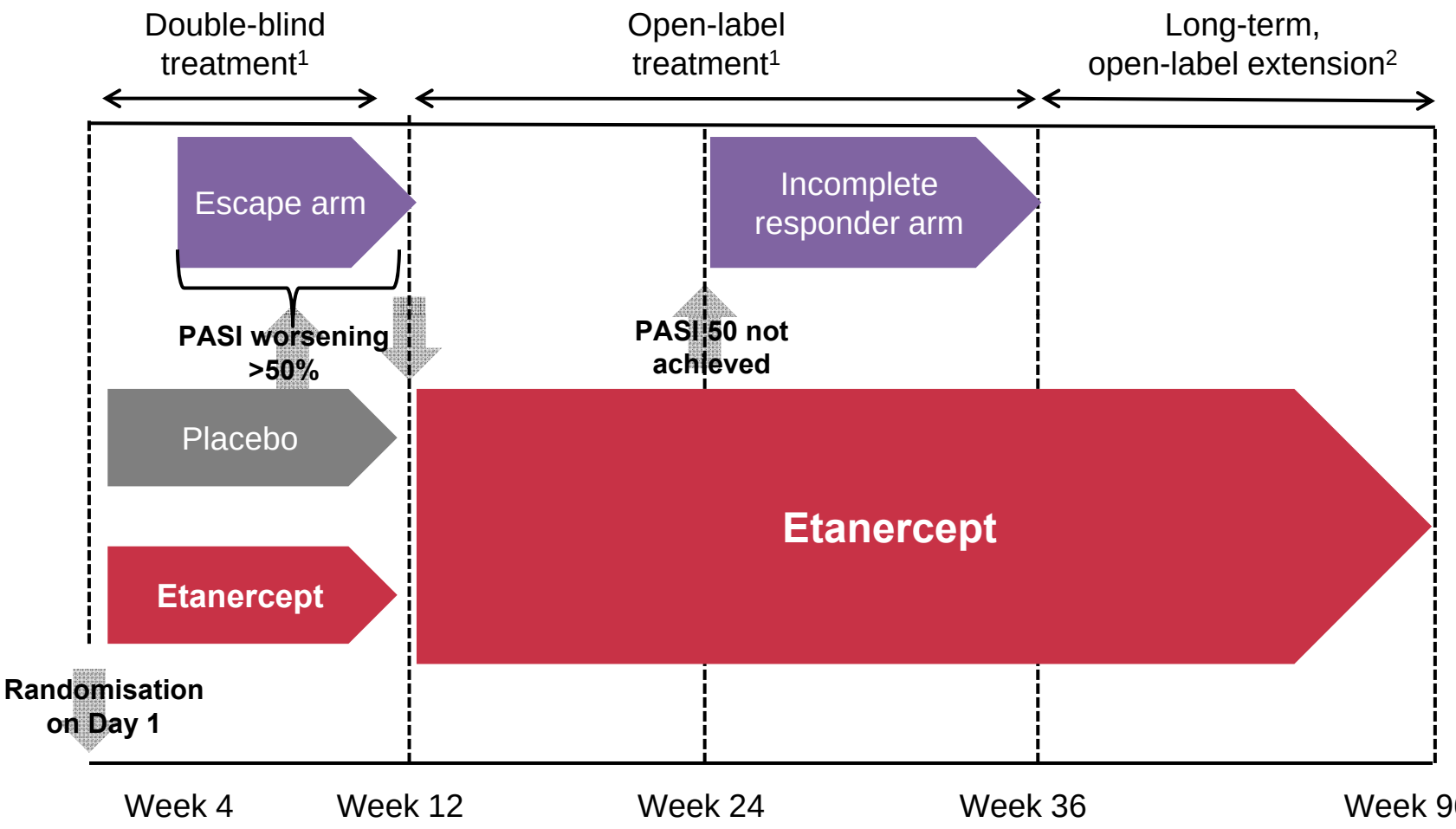
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Etanercept Treatment for Children and Adolescents with Plaque Psoriasis

Amy S. Paller, M.D., Elaine C. Siegfried, M.D., Richard G. Langley, M.D., Alice B. Gottlieb, M.D., Ph.D., David Pariser, M.D., Ian Landells, M.D., Adelaide A. Hebert, M.D., Lawrence F. Eichenfield, M.D., Vaishali Patel, Pharm.D., M.S., Kara Creamer, M.S., and Angelika Jahreis, M.D., Ph.D., for the Etanercept Pediatric Psoriasis Study Group*

Etanercept en psoriasis pediátrica

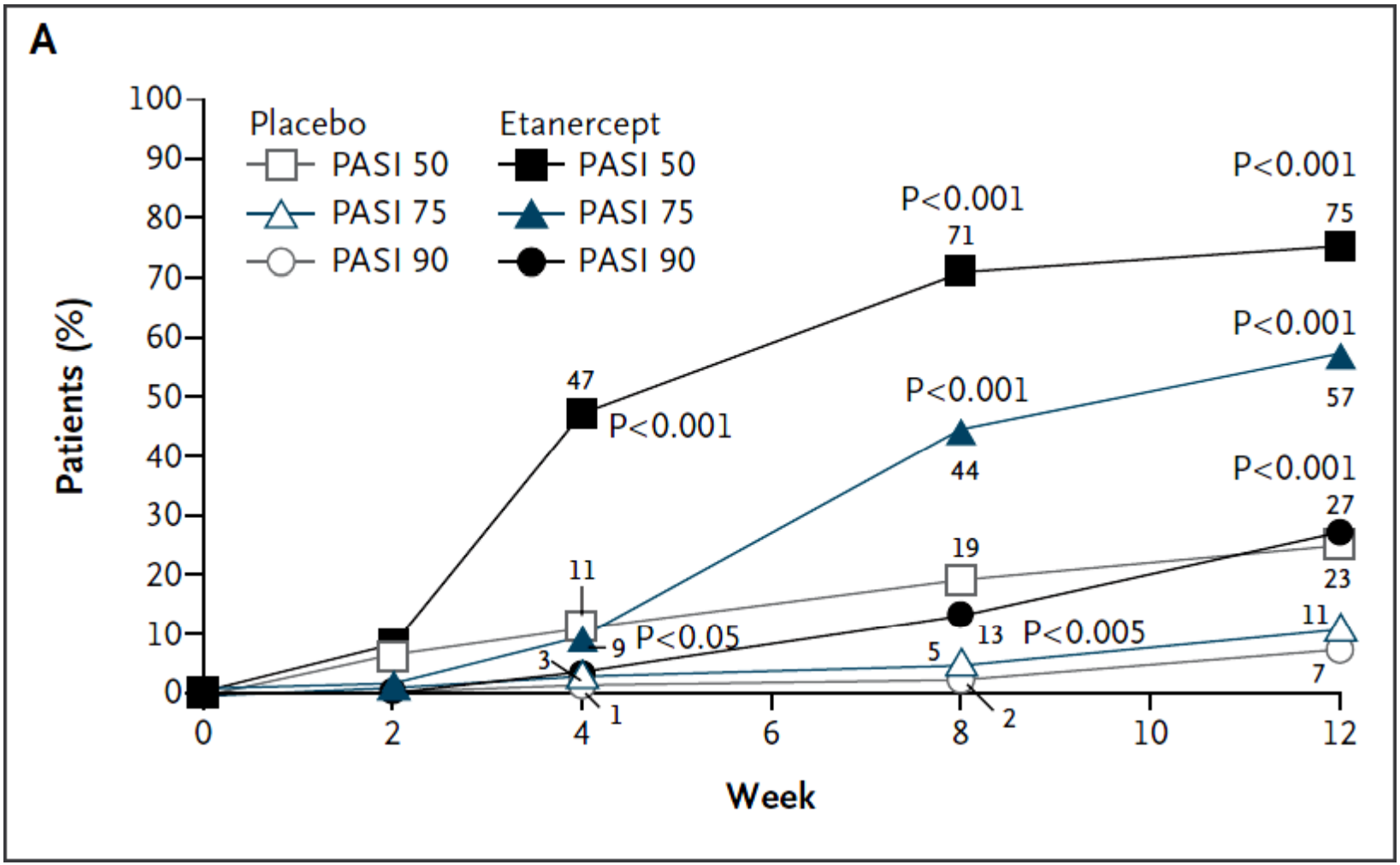


Study 211 enrolled patients aged 4–17 years (mean age 12.8 years to receive 0.8 mg/kg **Etanercept** QW

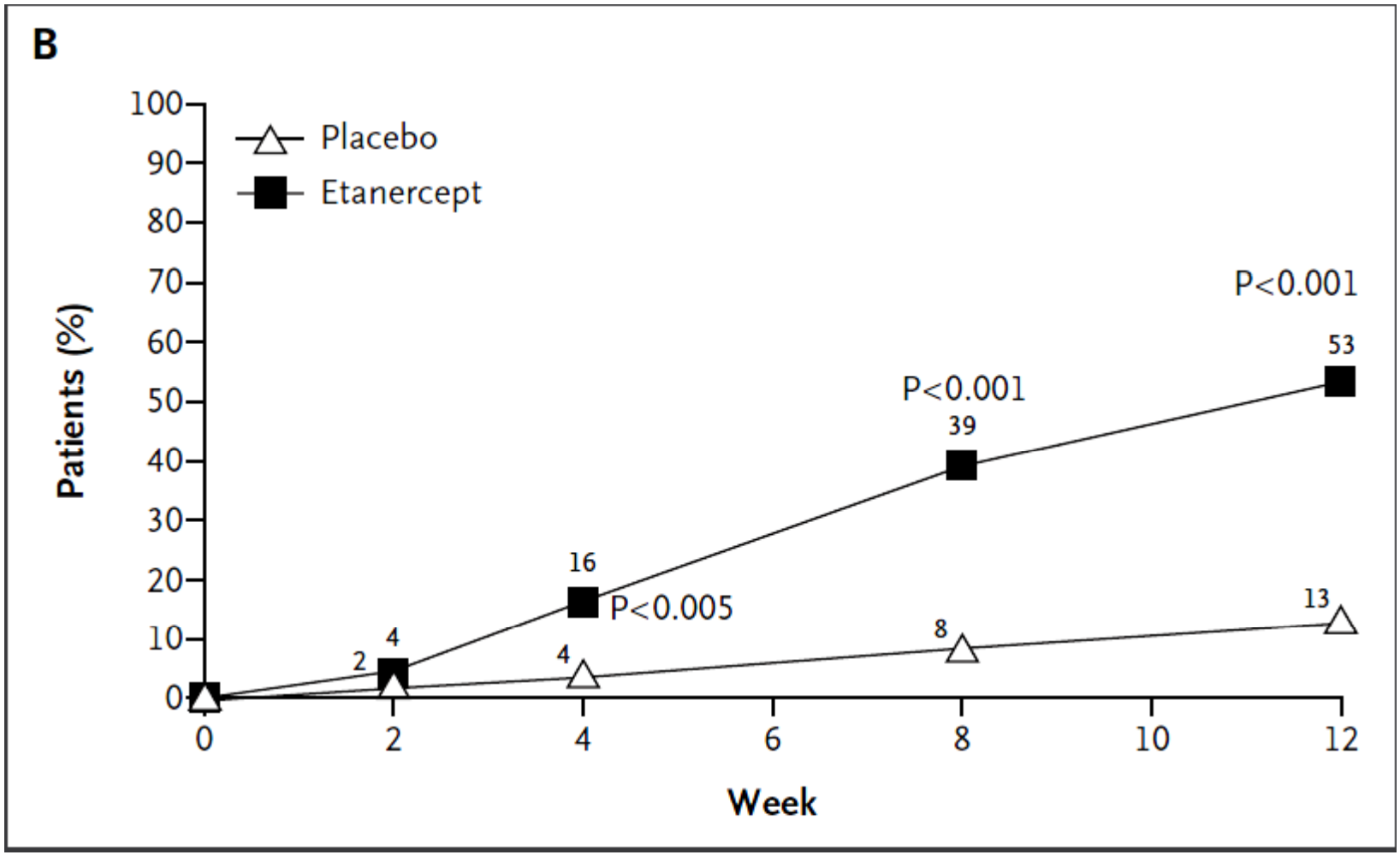
1. Langley RG, et al. J Am Acad Dermatol. 2011;64(1):64–70;
2. Paller, et al. J Am Acad Dermatol. 2010;63(5):762–8.

- PASI: Psoriasis Area Severity Index; QW: Once weekly

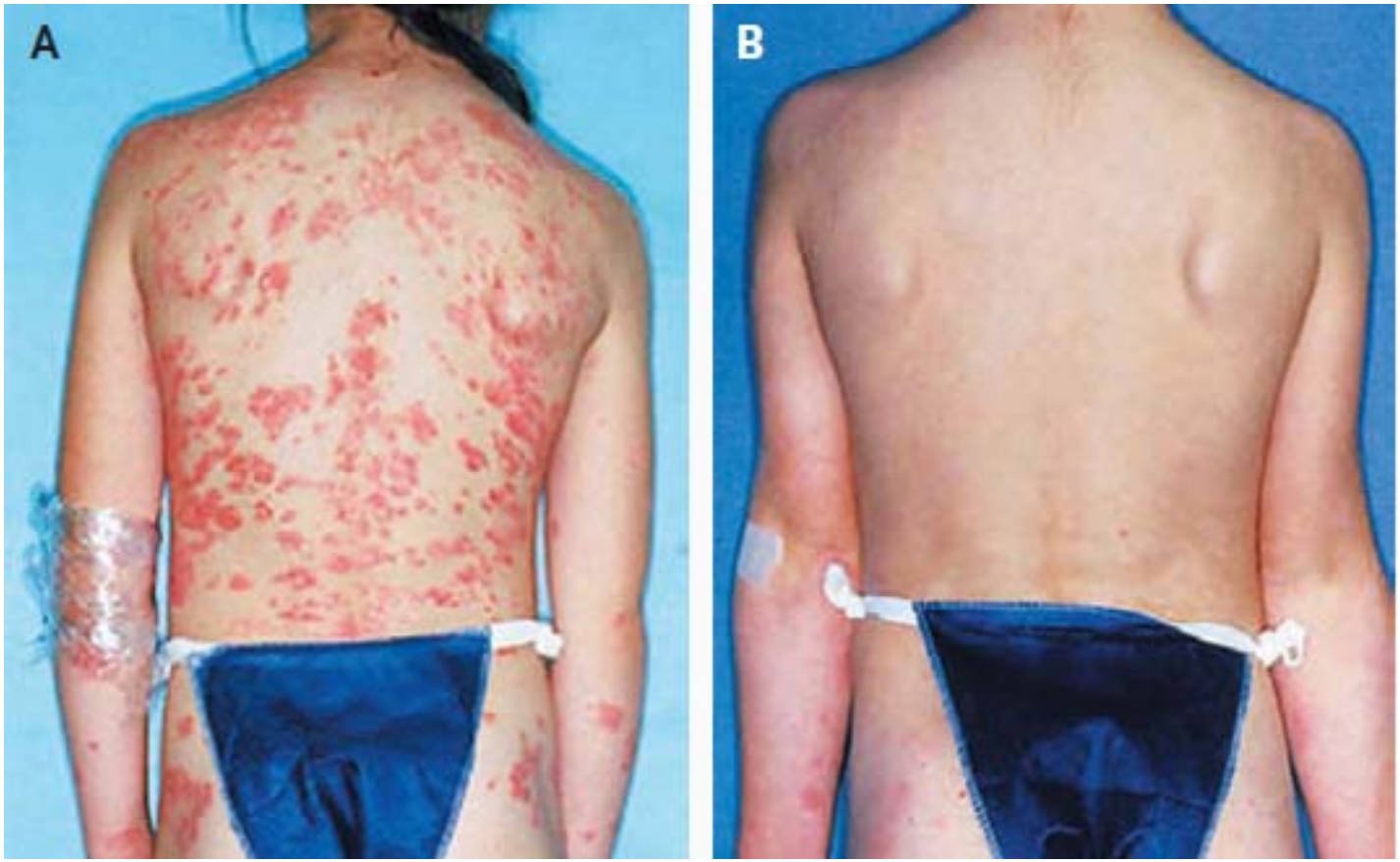
Etanercept Treatment for Children and Adolescents with Plaque Psoriasis



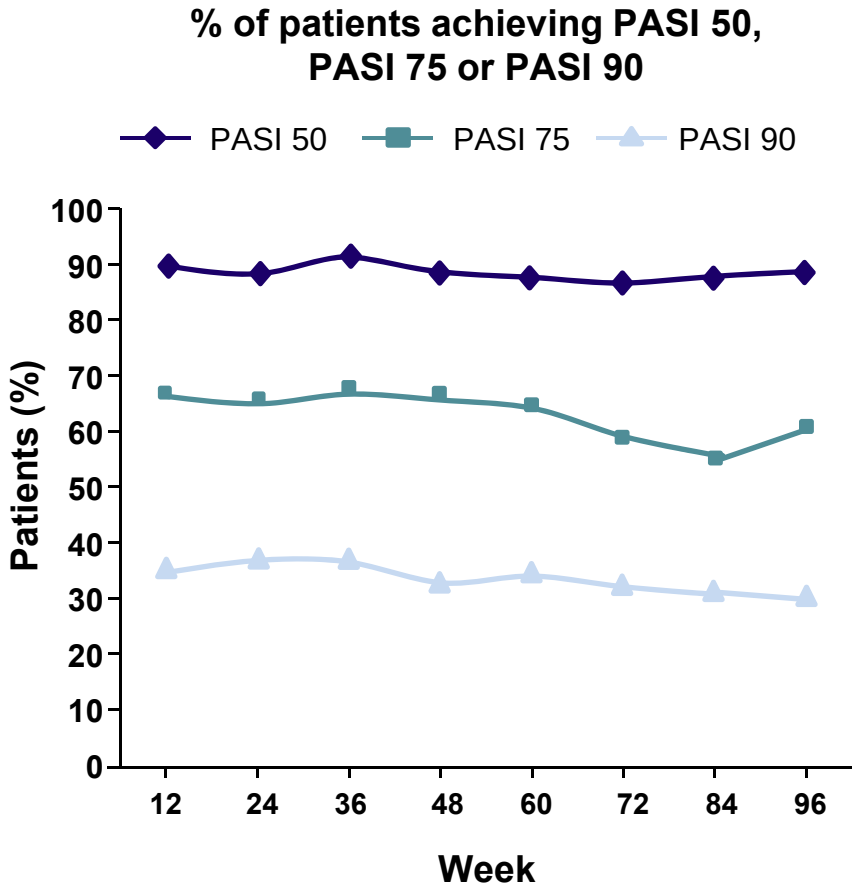
Etanercept Treatment for Children and Adolescents with Plaque Psoriasis

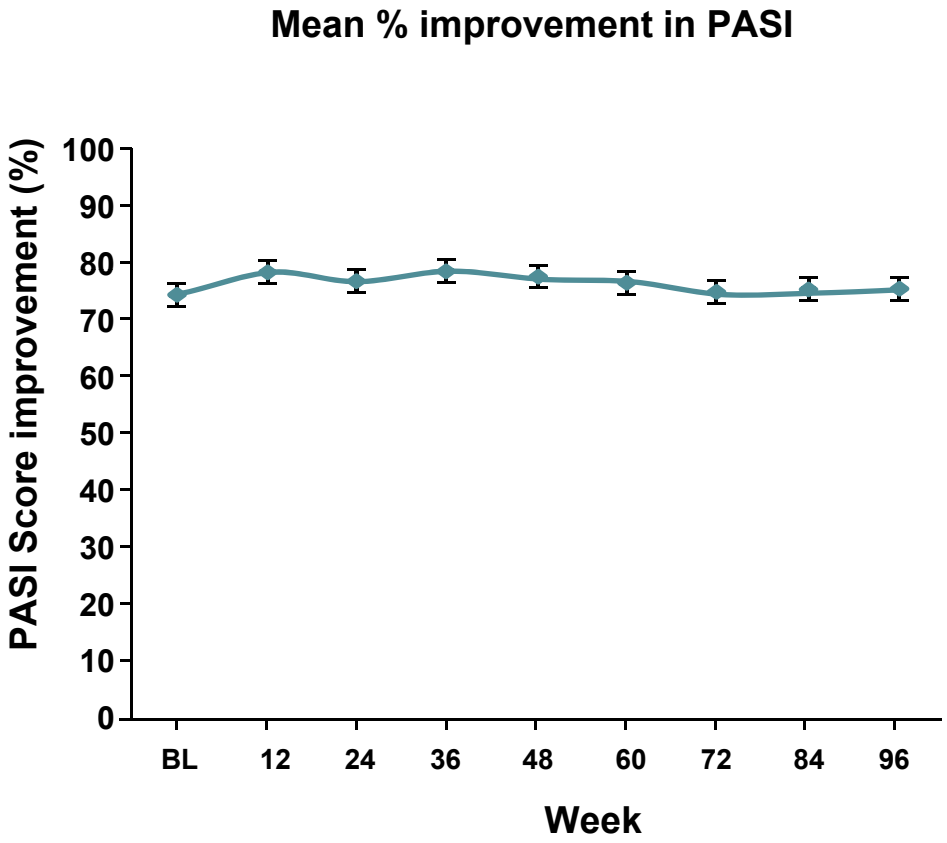


Etanercept Treatment for Children and Adolescents with Plaque Psoriasis



Etanercept en psoriasis pediátrica





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- PASI: Psoriasis Area Severity Index; QW: Once weekly

Seguridad a sem 96

Incidence and corresponding exposure-adjusted rates of adverse events occurring in ≥5% of patients on Etanercept (N=181)

Adverse event	Patients, n (%)	Events, n	Exposure-adjusted event rate/100 patient-years
Upper respiratory tract infection	45 (24.9)	68	19.1
Nasopharyngitis	31 (17.1)	49	13.8
Streptococcal pharyngitis	23 (12.7)	26	7.3
Headache	21 (11.6)	28	7.9
Sinusitis	19 (10.5)	23	6.5
Skin papilloma	12 (6.6)	17	4.8
Pyrexia	11 (6.1)	16	4.5
Cough	10 (5.5)	13	3.7
Pharyngolaryngeal pain	10 (5.5)	17	4.8
Acne	9 (5.0)	9	2.5
Nasal congestion	9 (5.0)	10	2.8
Pharyngitis	9 (5.0)	11	3.1

1. Langley RG, et al. J Am Acad Dermatol. 2011;64(1):64–70;
2. Paller, et al. J Am Acad Dermatol. 2010;63(5):762–8.

- PASI: Psoriasis Area Severity Index; QW: Once weekly

Five-Year Open-Label Extension Study of Safety and Efficacy of Etanercept in Children and Adolescents With Moderate to Severe Plaque Psoriasis

Amy S. Paller, MD,[1] Elaine C. Siegfried, MD,[2] David M. Pariser, MD,[3] Kara Creamer Rice, MS,[4] Mona Trivedi, MD,[4] Jan Iles, MD,[4] David H. Collier, MD,[4] Greg Kricorian, MD,[4] Richard G. Langley, MD[5]

[1]Northwestern University Feinberg School of Medicine and the Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA; [2]Cardinal Glennon Children's Hospital and Saint Louis University, St. Louis, MO, USA; [3]Eastern Virginia Medical School and Virginia Clinical Research, Inc., Norfolk, VA, USA; [4]Amgen Inc., Thousand Oaks, CA, USA; [5]Dalhousie University, Halifax, NS, Canada

Sponsored by Immunex, a wholly owned subsidiary of Amgen Inc. and by Wyeth, which was acquired by Pfizer in October 2009
Medical writing support provided by Dikran Toroser (Amgen Inc.) and Julia R. Gage (on behalf of Amgen Inc.)

J Am Acad Dermatol 2016;74:280-7.

Results

Safety

AEs Occurring in > 10% of Patients

AE	Patients[a] (n (%)	Events[b] n	Exposure-Adjusted Event Rate/100 Patient-Years
Upper respiratory tract infection	68 (37.6)	144	23.2
Nasopharyngitis	47 (26.0)	93	15.0
Headache	39 (21.5)	55	8.9
Acne	33 (18.2)	21	3.4
Streptococcal infection	27 (14.9)	36	5.8
Sinusitis	24 (13.3)	31	5.0
Skin papilloma	24 (13.3)	17	2.7
Cough	22 (12.2)	26	4.2
Influenza	21 (11.6)	28	4.5
Oropharyngeal pain	20 (11.0)	32	5.2

[a]Data represent the number of patients with an event at any time during the study, regardless of whether the patient was on or off etanercept at the time of the event. [b]Data represent the number of events that occurred during exposure to etanercept.

J Am Acad Dermatol 2016;74:280-7.

Results

Safety (Cont.)

Serious AEs

AE	Patients[a] (n (%)	Events[b] n	Exposure-Adjusted Event Rate/100 Patient-Years
Abortion induced	1 (0.6)	1	0.2
Anxiety	1 (0.6)	1	0.2
Cellulitis	1 (0.6)	1	0.2
Infectious mononucleosis	1 (0.6)	1	0.2
Osteonecrosis	1 (0.6)	2	0.3
Postoperative intestinal obstruction	1 (0.6)	1	0.2
Thyroid cyst	1 (0.6)	1	0.2

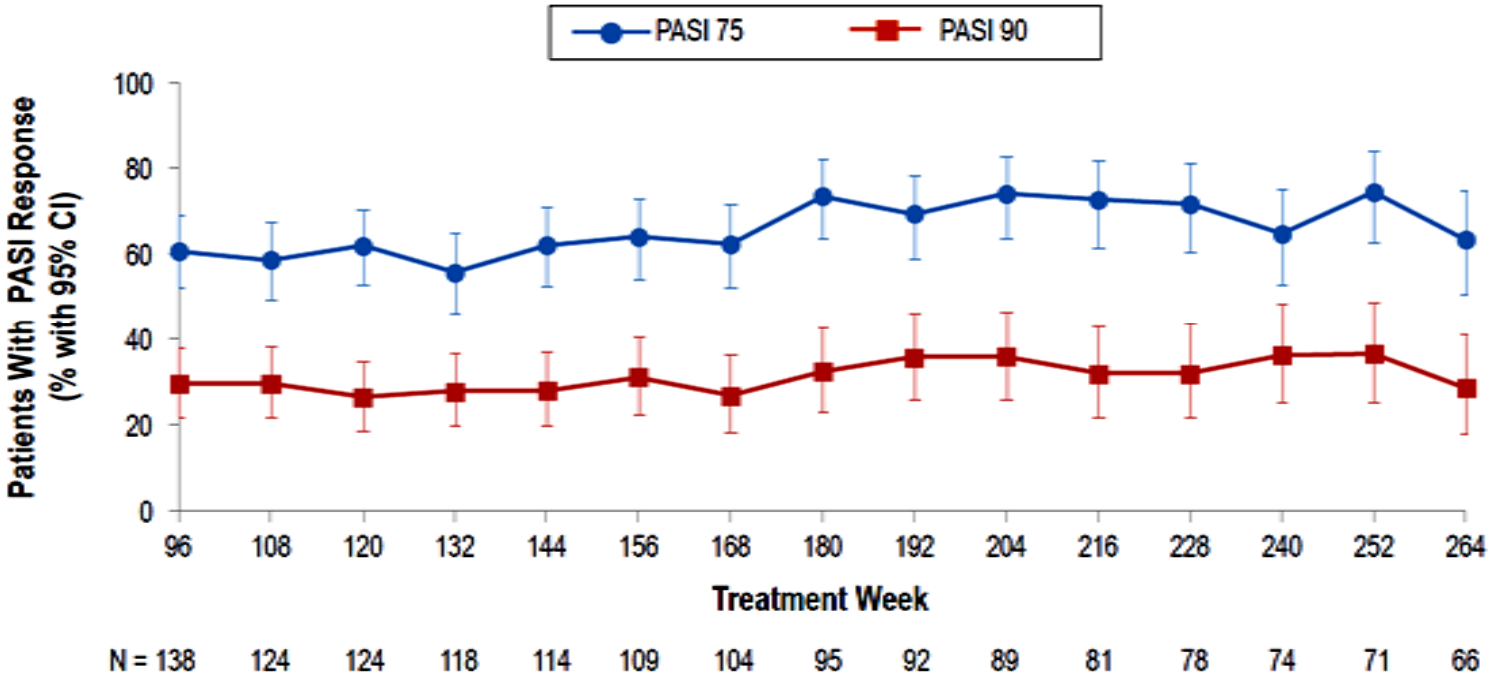
[a]Data represent the number of patients with an event at any time during the study, regardless of whether the patient was on or off etanercept at the time of the event. [b]Data represent the number of events that occurred during exposure to etanercept.

J Am Acad Dermatol 2016;74:280-7.

Results

Efficacy

PASI Responses (as observed)

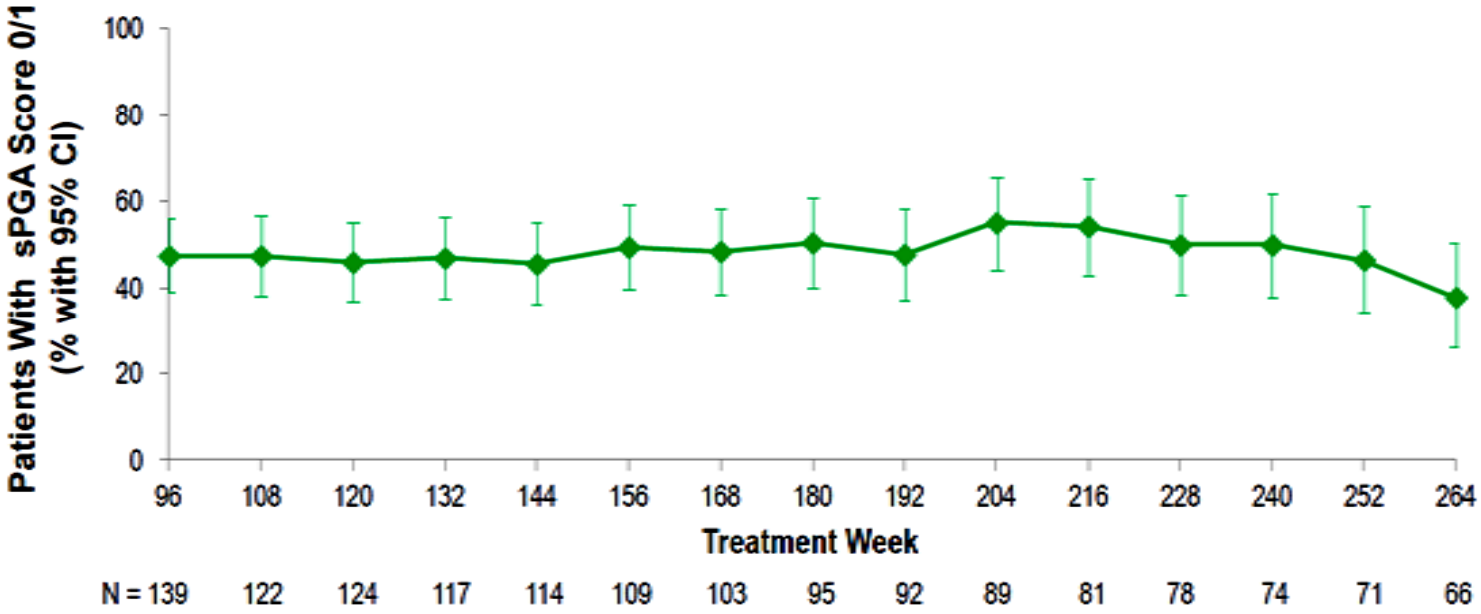


J Am Acad Dermatol 2016;74:280-7.

Results

Efficacy (Cont.)

sPGA Status of Clear/Almost Clear (as observed)

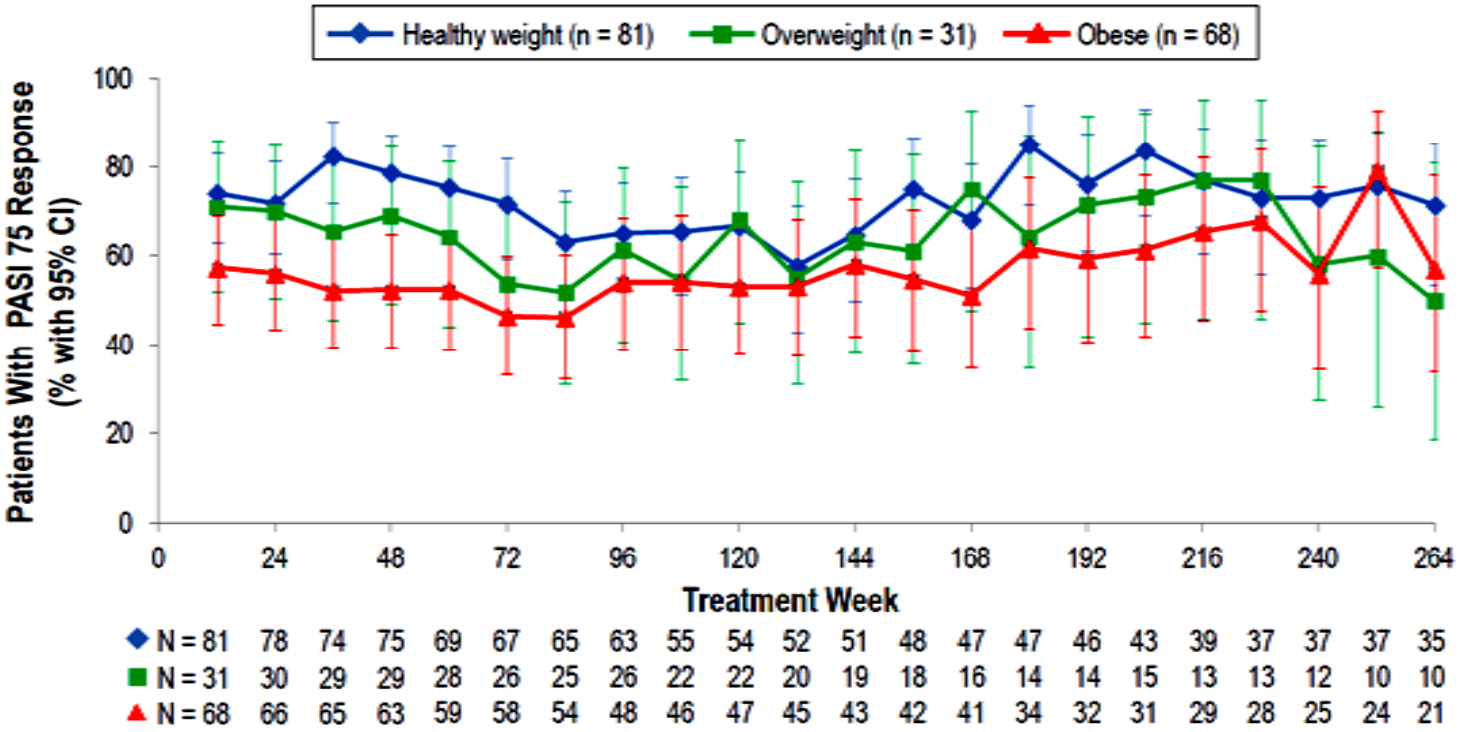


J Am Acad Dermatol 2016;74:280-7.

Results

Efficacy (Cont.)

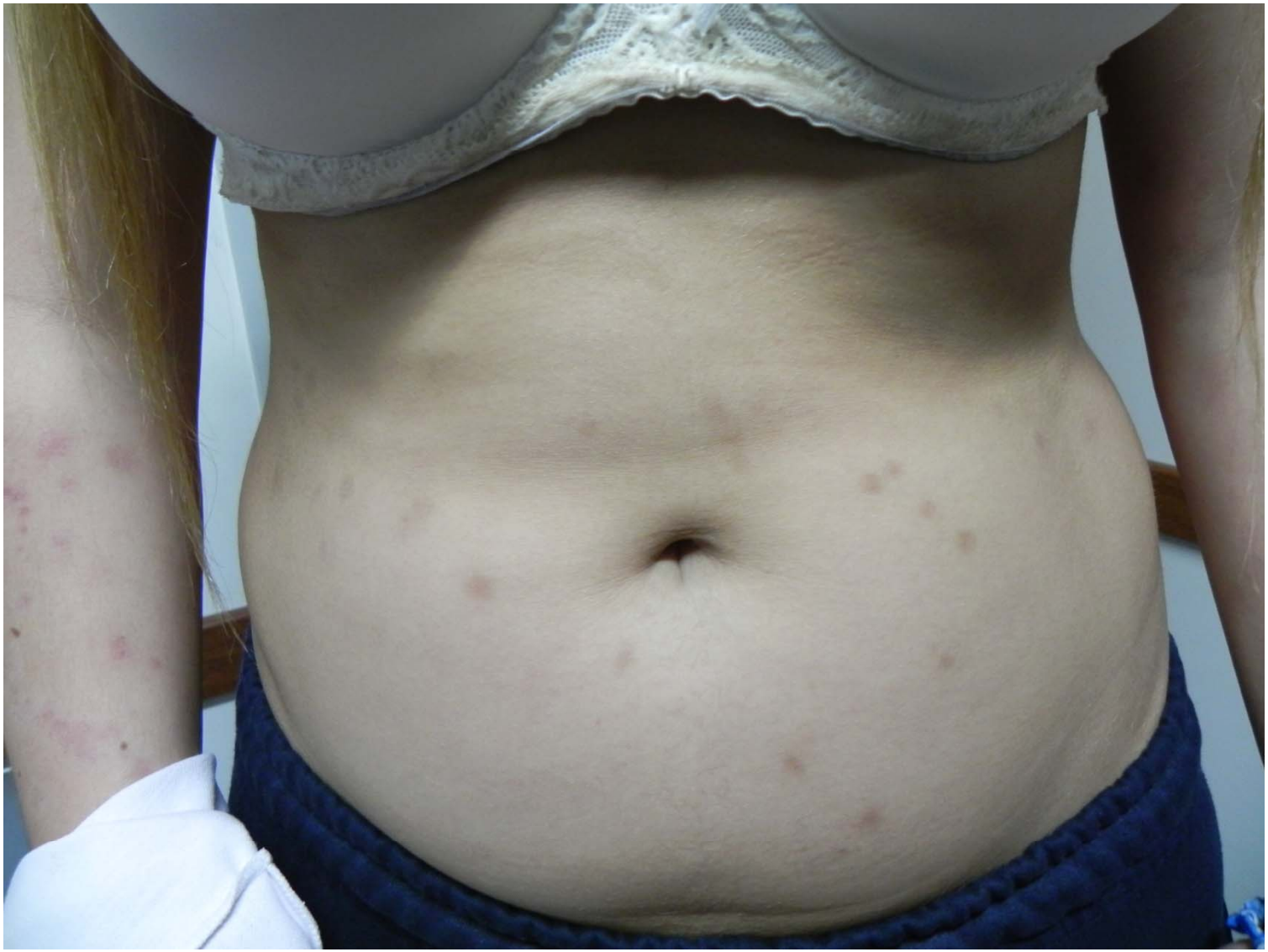
PASI Responses by BMI Category (as observed)



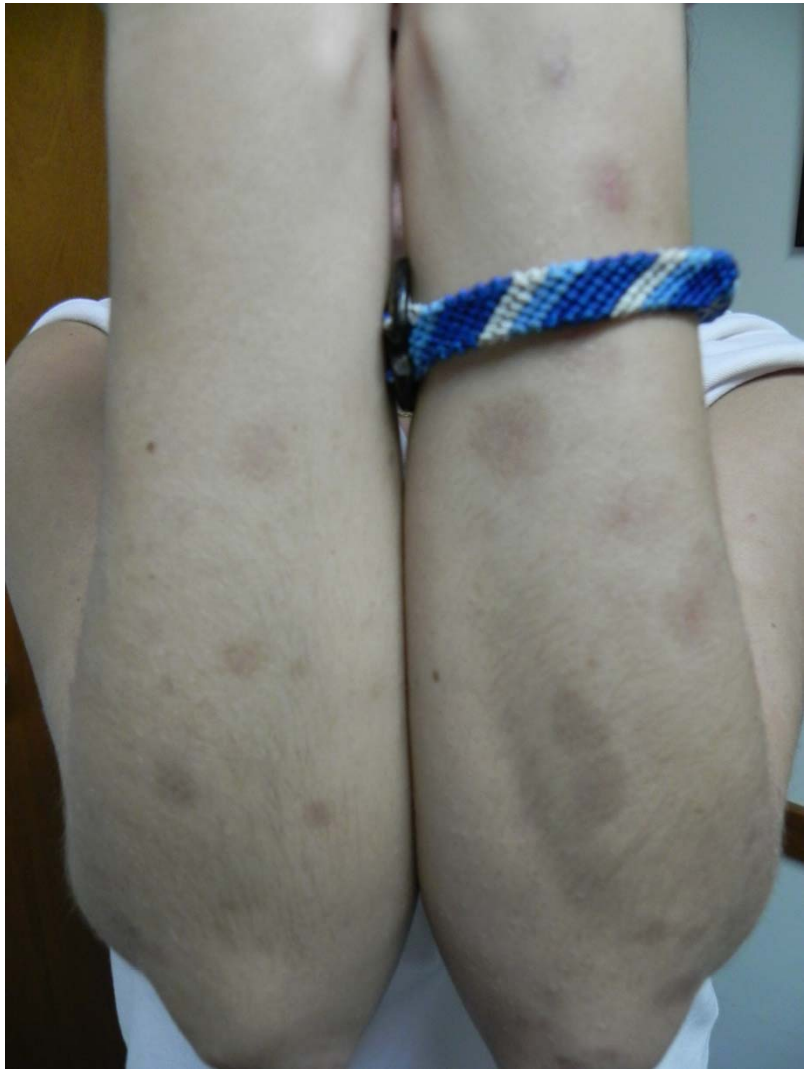
BMI percentile categories: 0 to 5th percentile = underweight; 5th to 84th percentile = healthy weight; 85th to 94th percentile = overweight; ≥ 95th percentile = obese

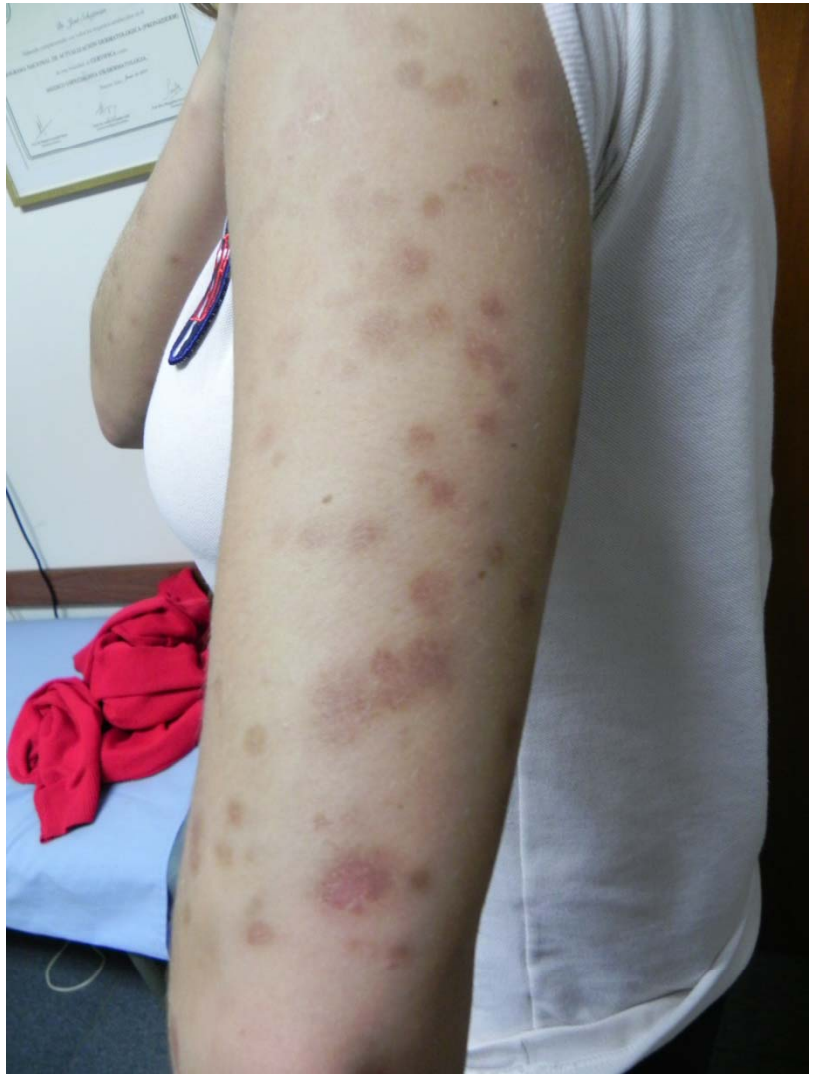
J Am Acad Dermatol 2016;74:280-7.

Etanercept + UVBnb

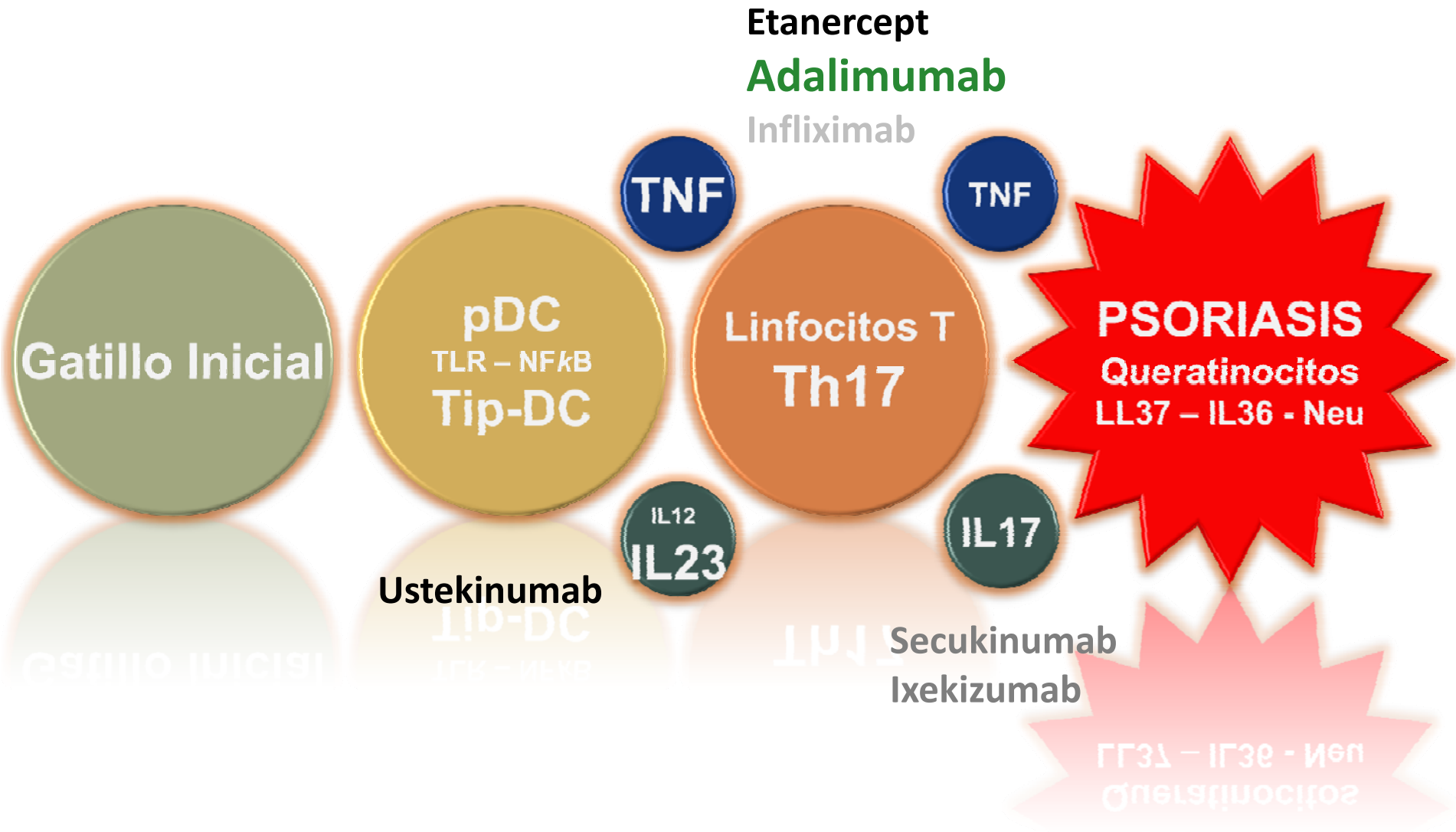


Etanercept + UVBnb





Blancos y biológicos en la psoriasis



Efficacy and Safety of Adalimumab Versus Methotrexate Treatment in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the 16-Week, Randomized, Double-Blind Period of a Phase 3 Study

Kim Papp, MD,[1,*] Diamant Thaçi, MD,[2] Danielle Marcoux, MD,[3] Lisa Weibel, MD,[4] Kristina Unnebrink, PhD,[5] David A. Williams, MD[6]

[1]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [2]Comprehensive Center for Inflammation Medicine, University Medical School Schleswig Holstein, Campus Lübeck, Germany; [3]CHU Sainte-Justine, Montreal, QC, Canada; [4]Pediatric Dermatology Department, University Children's Hospital, Zurich, Switzerland; [5]AbbVie Deutschland GmbH & Co KG, Ludwigshafen, Germany; [6]AbbVie Inc., North Chicago, IL, USA

*Presenting author

Poster to be presented at the 23rd World Congress of Dermatology; June 8–13, 2015; Vancouver, Canada

BACKGROUND

- Psoriasis (Ps) is a chronic inflammatory disease; approximately one third of Ps cases occur in pediatric patients[1]
- Adalimumab (ADA), a fully human monoclonal antibody directed against tumor necrosis factor (TNF), was recently approved in the European Union for the treatment of severe chronic plaque Ps in children and adolescents from 4 years of age who have had an inadequate response to or are contraindicated for topical therapy and phototherapies

OBJECTIVES

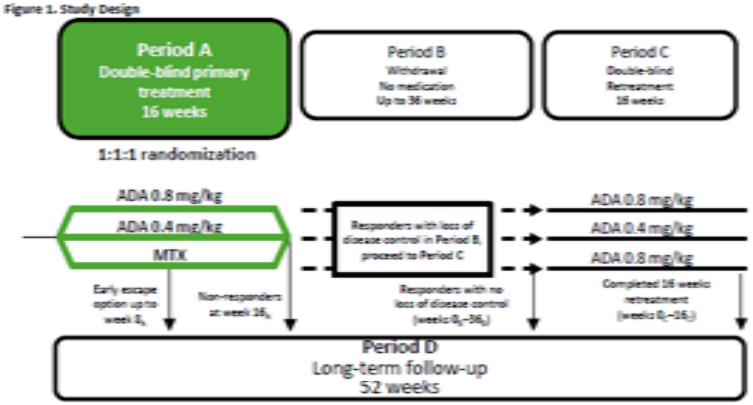
- This study evaluates the safety and efficacy of 2 dosing schedules of the TNF inhibitor ADA vs. methotrexate (MTX) in pediatric patients with severe chronic plaque Ps
- Results from the initial 16-week double-blind treatment period are presented here

METHODS

STUDY DESIGN

- This multicenter, randomized, double-blind study (NCT01251614) included 4 periods (Figure 1):

Figure 1. Study Design



ADA, adalimumab; MTX, methotrexate.

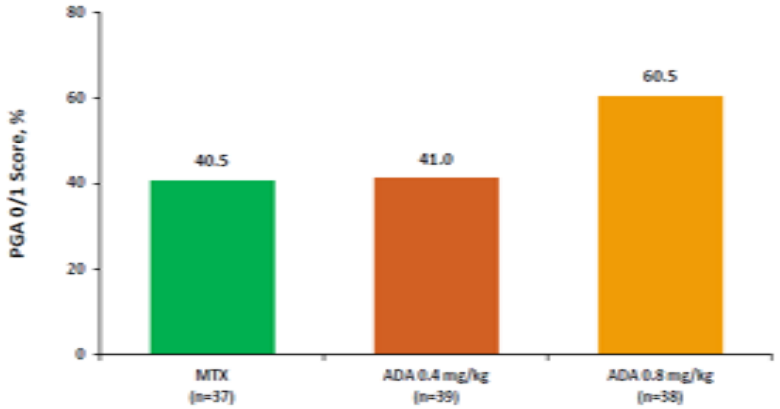
- Period A: 16-week double-blind treatment, in which patients were randomized 1:1:1 to
  - 0.8 mg/kg ADA up to 40 mg, then every other week (eow) from week 1;
  - 0.4 mg/kg ADA up to 20 mg, then eow from week 1; or
  - 0.1–0.4 mg/kg MTX weekly up to 25 mg per week
- Period B: treatment withdrawal for treatment responders in Period A
- Period C: ADA re-treatment of patients who lost disease control in Period B
- Period D: 52-week, long-term follow-up

PATIENTS

- Key inclusion criteria
  - Male and female pediatric patients (aged ≥4 to <18 years), with body weight ≥13 kg and a clinical diagnosis of chronic plaque Ps for ≥6 months were eligible
  - Patients must have failed topical therapy and required systemic therapy to control their disease
  - Inclusion criteria were at least 1 of the following :
    - Physician's Global Assessment (PGA) ≥4 (marked to severe Ps)
    - Body surface area (BSA) involved >20% (or BSA >10% and very thick lesions)
    - Psoriasis Area and Severity Index (PASI) >20
    - PASI >10 and at least 1 of the following:
      - Active psoriatic arthritis unresponsive to non-steroidal anti-inflammatory drugs

- Approximately 20% more patients receiving 0.8 mg/kg ADA achieved a PGA 0/1 at week 16 (60.5%) than patients receiving MTX (40.5%; $P = 0.083$) or 0.4 mg/kg ADA (41.0%; $P = 0.087$; Figure 3)
  - The magnitude of the treatment effect with 0.8 mg/kg AA is considered clinically relevant

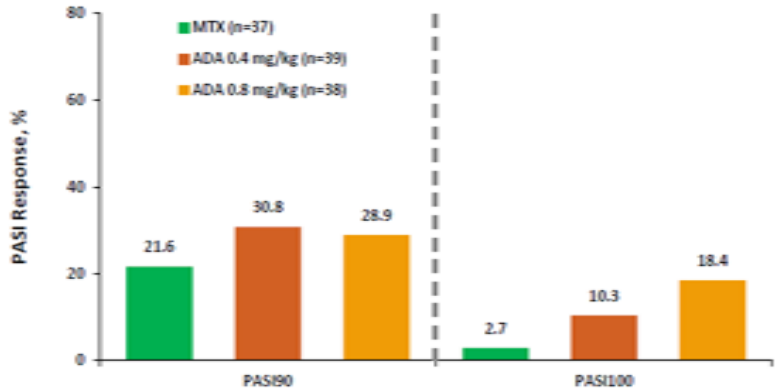
Figure 3. PGA 0/1 Score at Week 16



ADA, adalimumab; MTX, methotrexate; PGA, Physician's Global Assessment. PGA 0/1 is defined as PGA clear or minimal.

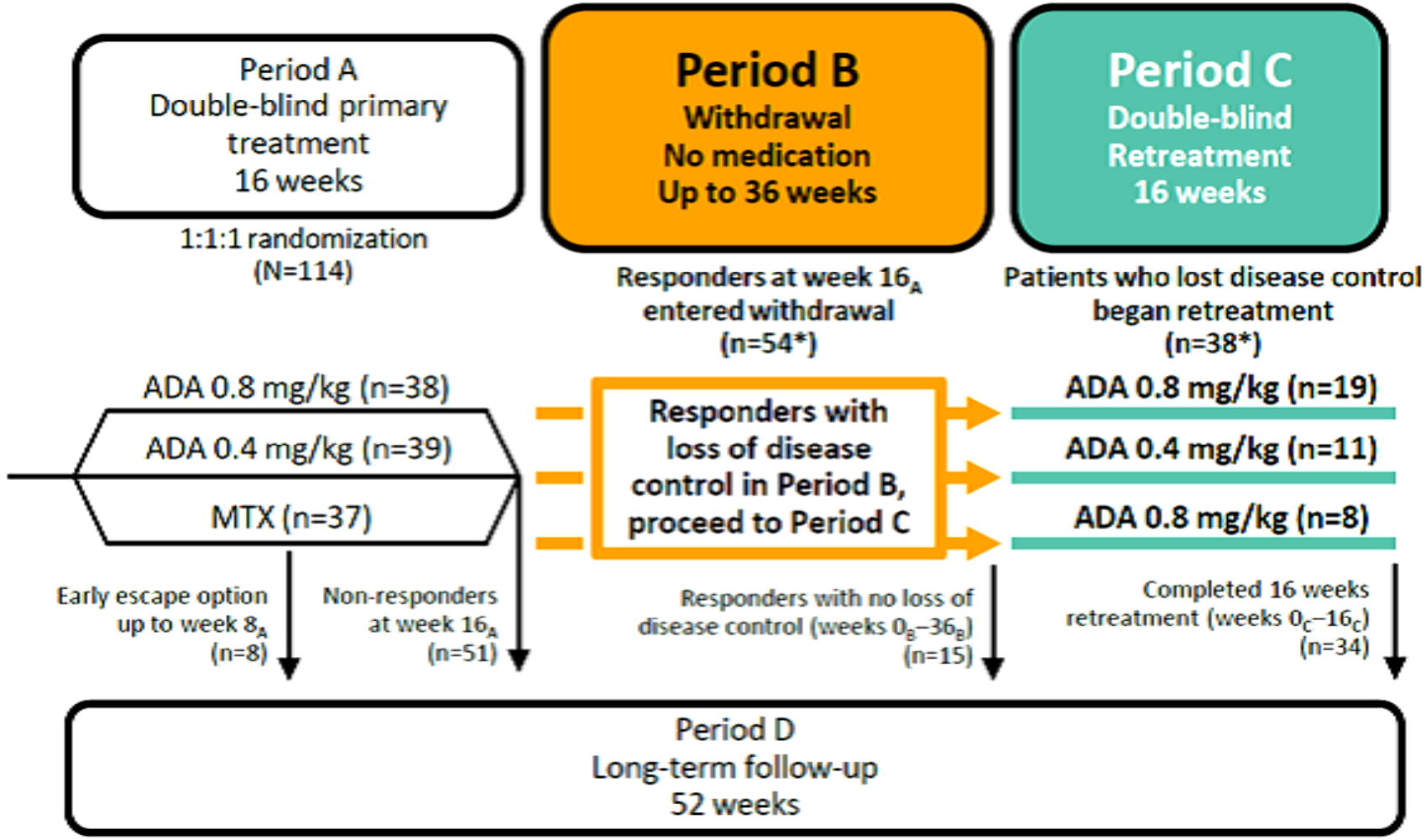
- Patients treated with 0.8 mg/kg ADA achieved PASI75 and PGA 0/1 responses earlier than patients treated with MTX: at week 4, PASI75 response rates were 23.7% and 0%, respectively, and PGA 0/1 response rates were 28.9% vs. 8.1%
- A numerically higher proportion of patients receiving 0.8 mg/kg ADA achieved a PASI90 or PASI100 response at week 16 than patients receiving MTX (Figure 4)

Figure 4. PASI90/100 Responses at Week 16



Efficacy and Safety of Adalimumab Versus Methotrexate Treatment in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the 16-Week, Randomized, Double-Blind Period of a Phase 3 Study

Figure 1. Study Design and Patient Disposition



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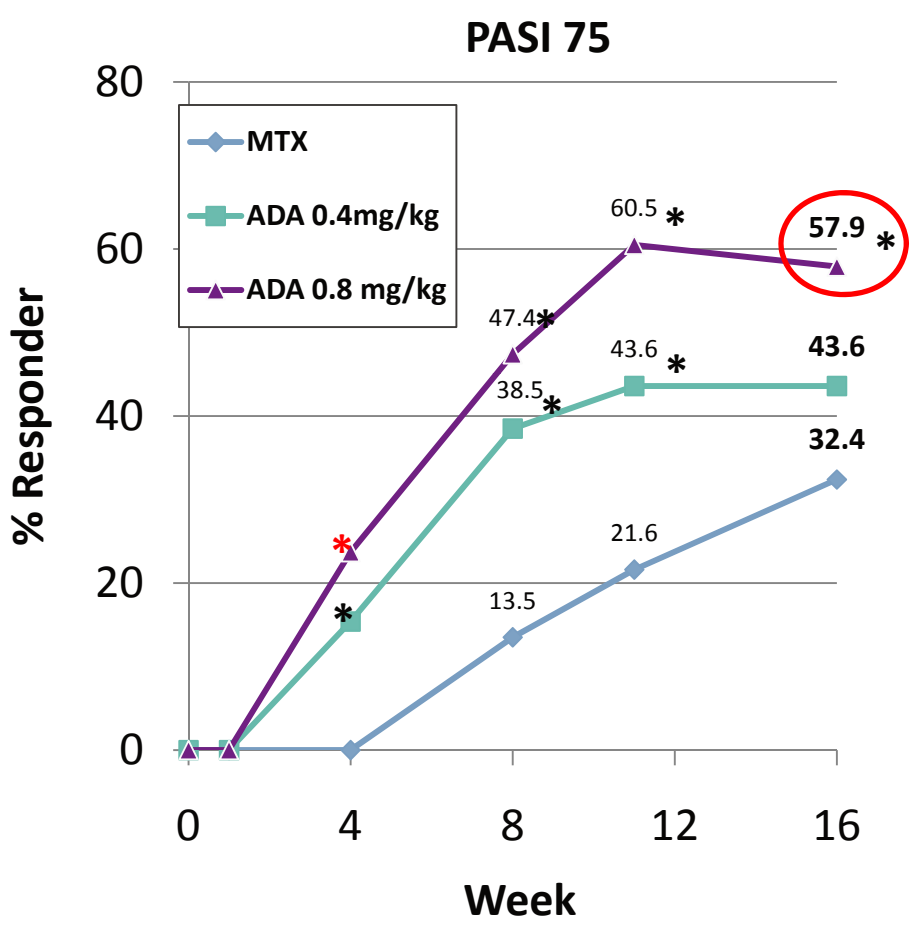
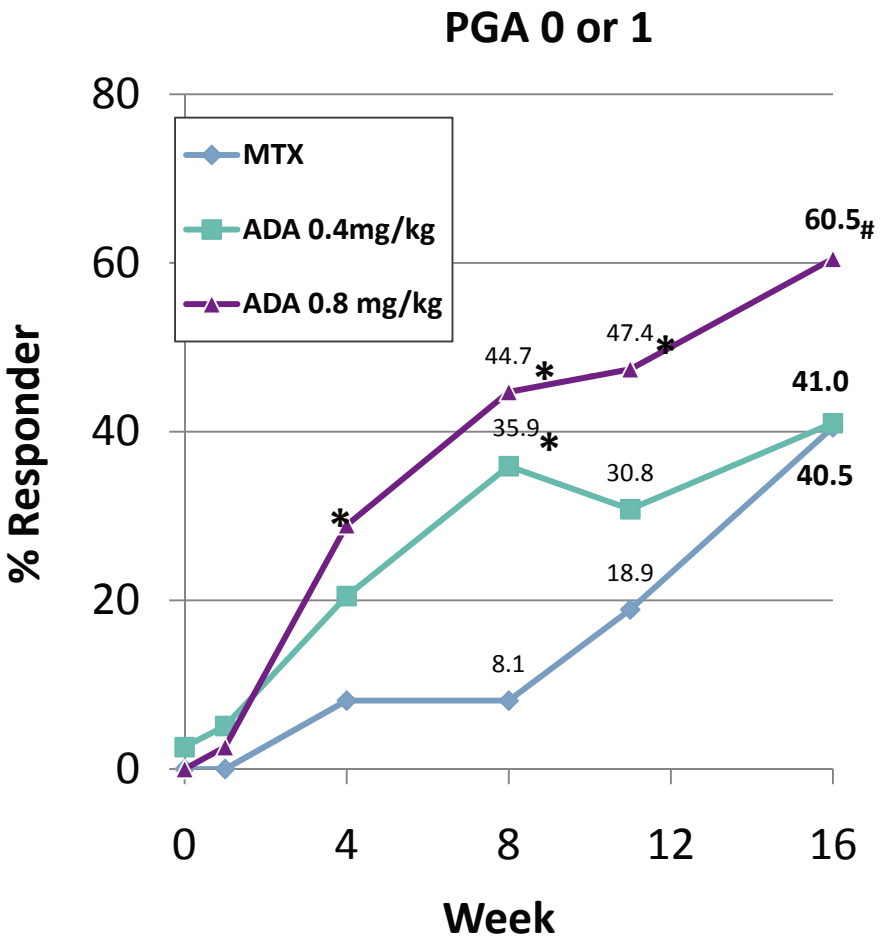
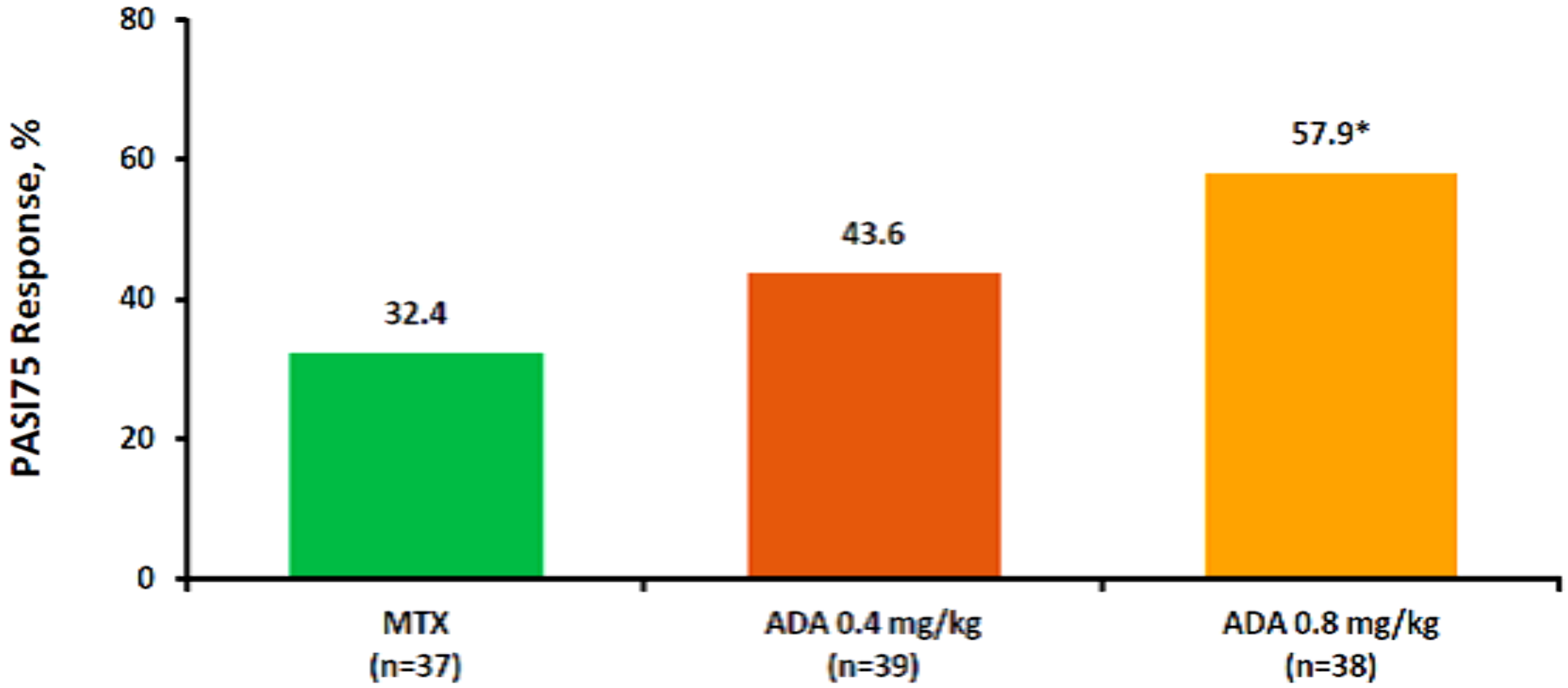




ITT, NRI Analysis * $p<0.05$ vs MTX; CAVE: # $p=0.083$ vs MTX

Efficacy and Safety of Adalimumab Versus Methotrexate Treatment in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the 16-Week, Randomized, Double-Blind Period of a Phase 3 Study

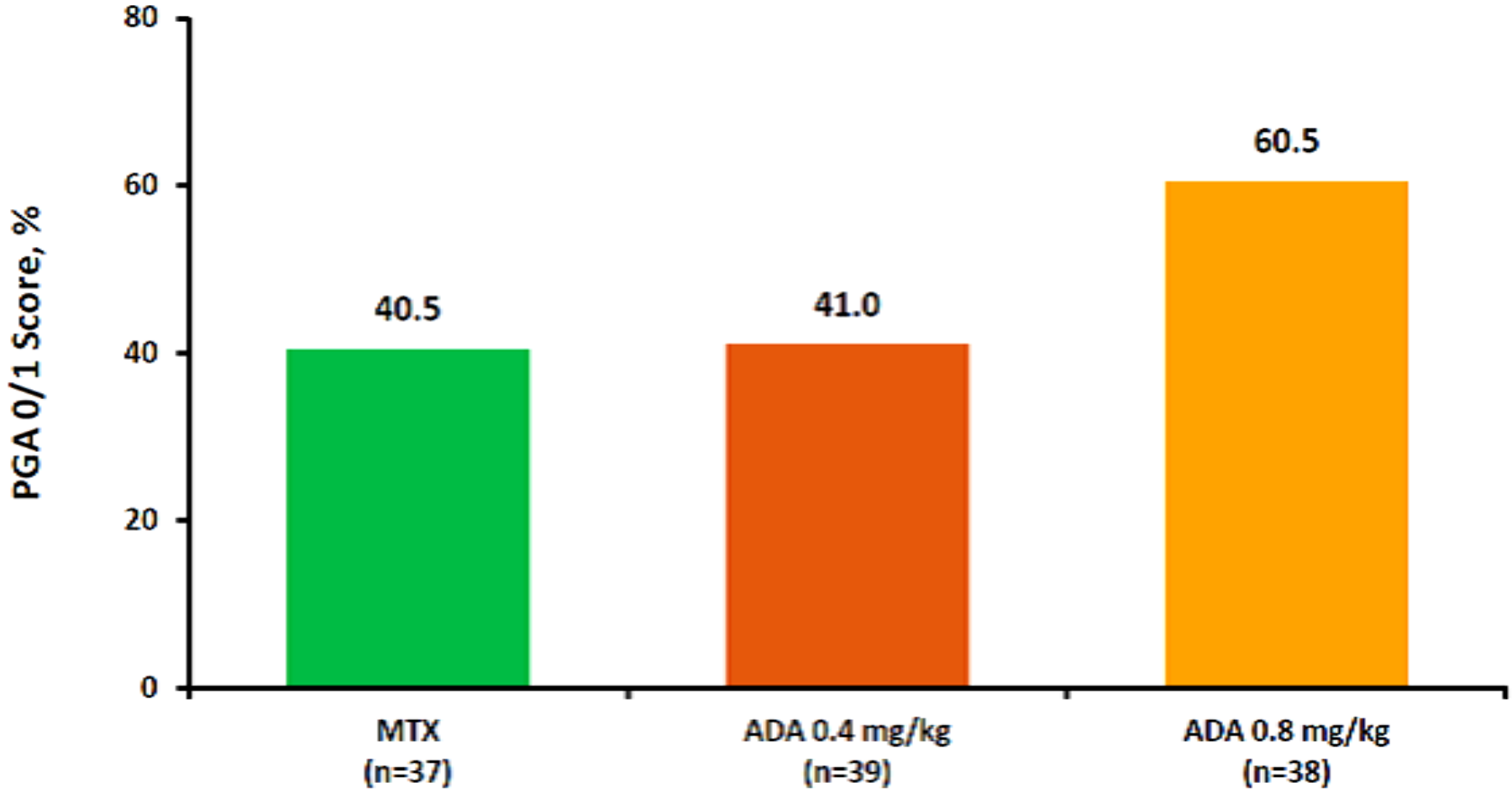
Figure 2. PASI75 Response at Week 16



ADA, adalimumab; MTX, methotrexate; PASI75, ≥75% improvement in Psoriasis Area and Severity Index.
*P<0.05 ADA 0.8 mg/kg vs. MTX.

Efficacy and Safety of Adalimumab Versus Methotrexate Treatment in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the 16-Week, Randomized, Double-Blind Period of a Phase 3 Study

Figure 3. PGA 0/1 Score at Week 16



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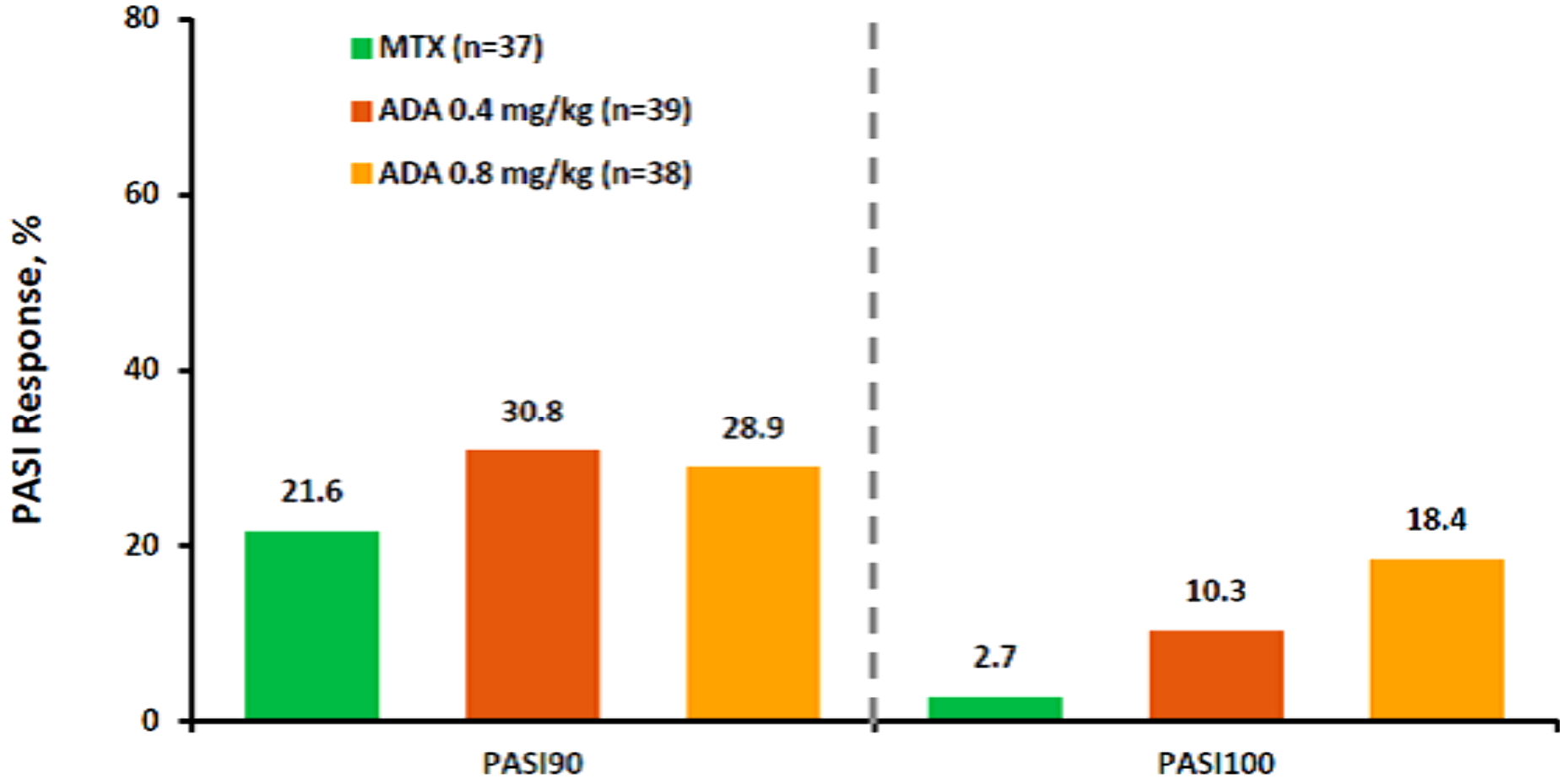
Efficacy and Safety of Adalimumab Versus Methotrexate Treatment in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the 16-Week, Randomized, Double-Blind Period of a Phase 3 Study

Figure 4. PASI90/100 Responses at Week 16



ADA, adalimumab; MTX, methotrexate; PASI90/100, ≥90%/100% improvement in Psoriasis Area and Severity Index.

Efficacy and Safety of Adalimumab Versus Methotrexate Treatment in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the 16-Week, Randomized, Double-Blind Period of a Phase 3 Study

Table 2: Adverse Events

AE, n (%)	MTX (n=37)	Adalimumab 0.4 mg/kg (n=39)	Adalimumab 0.8 mg/kg (n=38)	Total (N=114)
Any AE	28 (75.7)	30 (76.9)	26 (68.4)	84 (73.7)
Any severe AE	2 (5.4)	5 (12.8)	1 (2.6)	8 (7.0)
Any serious AE	0	3 (7.7)	0	3 (2.6)
Any serious AE at least possibly related to study drug	0	0	0	0
Any AE leading to discontinuation	0	0	0	0
Death	0	0	0	0
All infections	20 (54.1)	22 (56.4)	18 (47.4)	60 (52.6)
Serious infection	0	1 (2.6)	0	1 (0.9)
Malignancy	0	0	0	0
Allergic reaction	2 (5.4)	1 (2.6)	0	3 (2.6)
Injection site reaction	3 (8.1)	3 (7.7)	4 (10.5)	10 (8.8)

AE, adverse event; MTX, methotrexate. [a]Evaluated in all patients who received≥1 dose of study drug.

Efficacy and Safety of Adalimumab Versus Methotrexate in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the Treatment Withdrawal and Double-Blind Retreatment Periods of a Phase 3 Study

Sandra Philipp, MD,[1] Pierre-Dominique Ghislain, MD,[2] Ian Landells, MD,[3] Kristina Unnebrink, PhD,[4] David A. Williams, MD[5,*]

[1]Charité Universitätsmedizin Berlin, Berlin, Germany; [2]UCL St. Luc, Brussels, Belgium; [3]Nexus Clinical Research and Memorial University of Newfoundland, St. John's, Newfoundland, Canada; [4]AbbVie Deutschland GmbH & Co KG, Ludwigshafen, Germany; [5]AbbVie Inc., North Chicago, IL, United States.

*Presenting author

Poster to be presented at the 23rd World Congress of Dermatology; June 8–13, 2015; Vancouver, Canada

BACKGROUND

- Psoriasis (Ps) is a chronic inflammatory disease; approximately one third of Ps cases occur in children[1]
- Adalimumab (ADA), a fully human, monoclonal antibody directed against tumor necrosis factor (TNF), was recently approved in the European Union for the treatment of severe chronic plaque Ps in children and adolescents from 4 years of age who have had an inadequate response or are contraindicated for topical therapy and phototherapies

OBJECTIVES

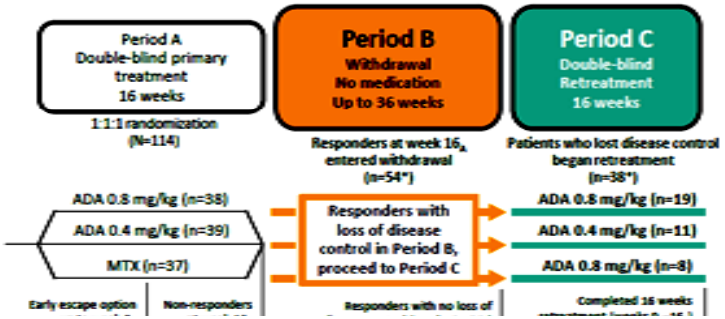
- This study is evaluating the safety and efficacy of 2 dosing schedules of the TNF inhibitor ADA compared with treatment with methotrexate (MTX) in pediatric patients with severe chronic plaque Ps
- Here, we report results from the treatment-withdrawal and double-blind retreatment periods

METHODS

STUDY DESIGN

- This multicenter, randomized, double-dummy, double-blind study (NCT01251614) included 4 periods **(Figure 1)**
  - **Period A:** 16-week double-blind treatment in which patients were randomized 1:1:1
    - 0.8 mg/kg ADA up to 40 mg, then every other week (eow) from week 1;
    - 0.4 mg/kg ADA up to 20 mg, then eow from week 1; or
    - 0.1–0.4 mg/kg MTX weekly up to 25 mg/week
  - **Period B:** treatment responders (patients achieving both ≥PASI 75 and PGA 0/1) from Period A were withdrawn from active treatment and monitored for loss of disease control, defined as a worsening of PGA score by ≥2 grades compared with week 16 of Period A, for up to 36 weeks
    - Patients who lost disease control entered the retreatment phase (Period C) at the time control was lost
    - Patients without loss of disease control completed Period B and then entered Period D, off treatment
  - **Period C:** Patients who experienced loss of disease control in Period B received blinded ADA retreatment according to their initial dose assignment (patients initially randomized to treatment with MTX received 0.8 mg/kg ADA)
    - Patients completing Period C entered Period D and received blinded ADA treatment
  - **Period D:** 52-week, long-term follow-up

Figure 1. Study Design and Patient Disposition



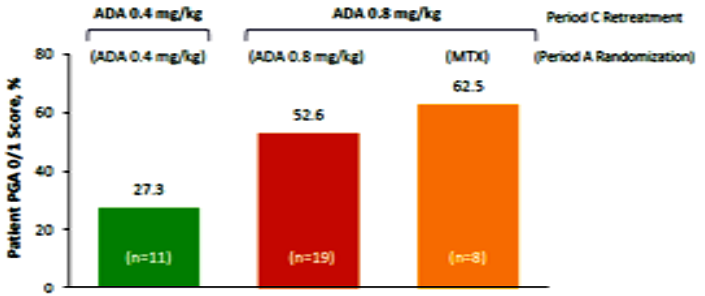
PERIOD B EFFICACY

- 47.4% of patients (54/114) were responders in Period A and entered Period B (MTX, 35.1% [13/37]; 0.4 mg/kg ADA, 46.2% [18/39]; 0.8 mg/kg ADA, 60.5% [23/38]; **Figure 1**)
- Time to loss of disease control after treatment withdrawal was numerically shorter for patients initially randomized to treatment with 0.8 mg/kg ADA in Period A (median, 118 days) vs. MTX (median, 184 days) or 0.4 mg/kg ADA (median, 217 days)

PERIOD C EFFICACY

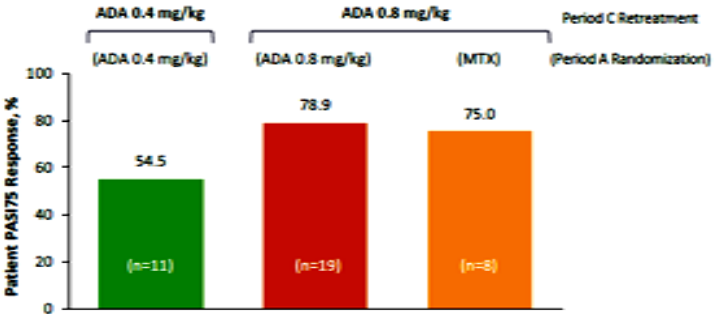
- 70.4% of patients (38/54) in Period B lost disease control and entered Period C
- No patients had a PGA 0/1 at Week 0 of Period C
- After 16 weeks of retreatment, 5/8 patients who responded to treatment with MTX in Period A and who subsequently lost disease control in Period B re-achieved a PGA 0/1 score after treatment with ADA 0.8 mg/kg, as did 10/19 and 3/11 patients who were initial responders to 0.8 and 0.4 mg/kg ADA, respectively **(Figure 2)**
- A PASI75 response was achieved in 6/8 patients who responded to treatment with MTX in Period A and who subsequently lost disease control in Period B, and 15/19 and 6/11 patients who were initial responders to 0.8 and 0.4 mg/kg ADA, respectively **(Figure 3)**

Figure 2. PGA 0/1 Score at Week 16 of Retreatment Period C



ADA, adalimumab; MTX, methotrexate; PGA, Physician Global Assessment.

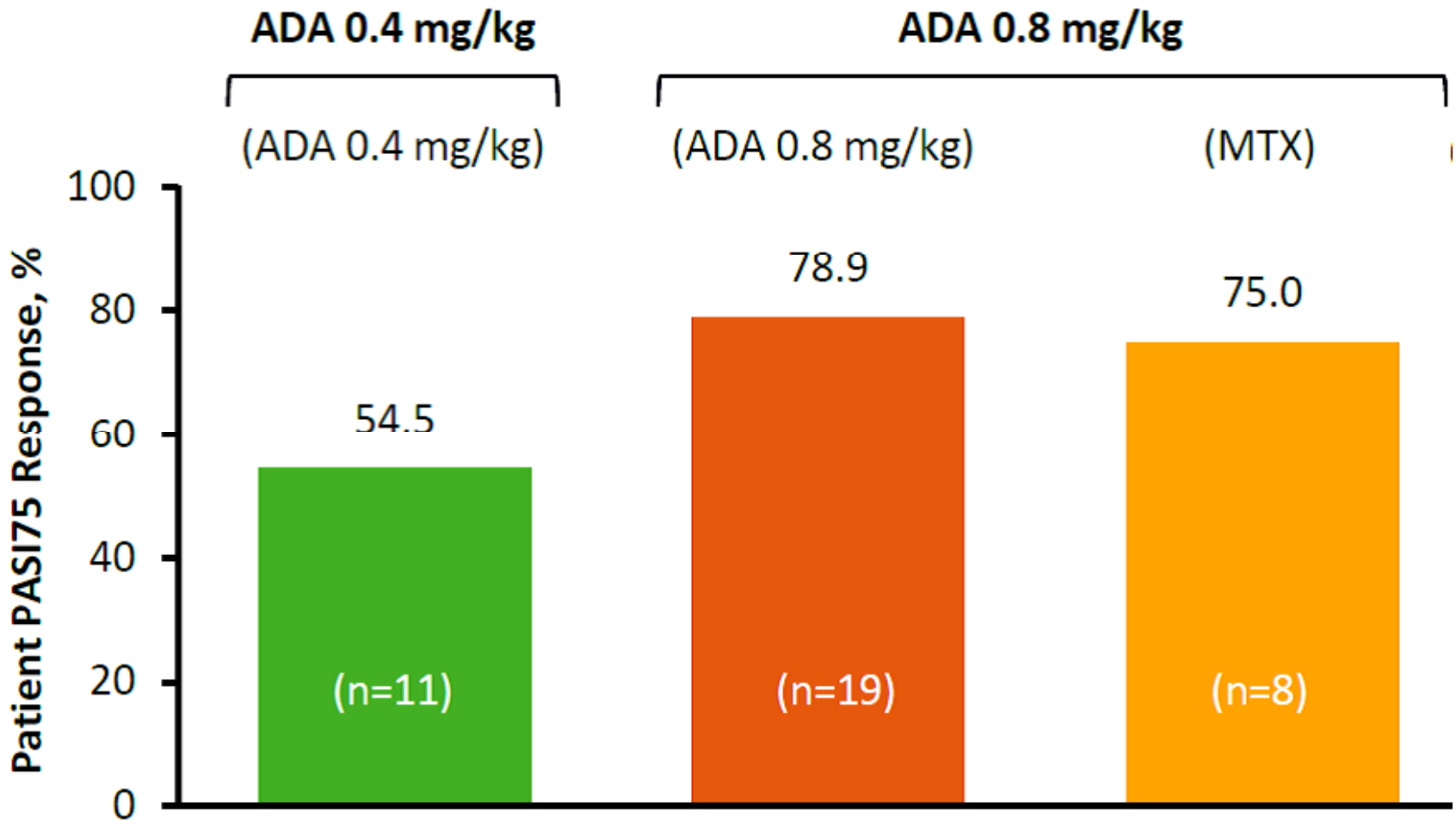
Figure 3. PASI75 Response at Week 16 of Retreatment Period C



ADA, adalimumab; MTX, methotrexate; PASI75, ≥75% improvement in Psoriasis Area and Severity Index.

Efficacy and Safety of Adalimumab Versus Methotrexate Treatment in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the 16-Week, Randomized, Double-Blind Period of a Phase 3 Study

Figure 3. PASI75 Response at Week 16 of Retreatment Period C



ADA, adalimumab; MTX, methotrexate; PASI75,≥75% improvement in Psoriasis Area and Severity Inde

Efficacy and Safety of Adalimumab Versus Methotrexate Treatment in Pediatric Patients With Severe Chronic Plaque Psoriasis: Results From the 16-Week, Randomized, Double-Blind Period of a Phase 3 Study

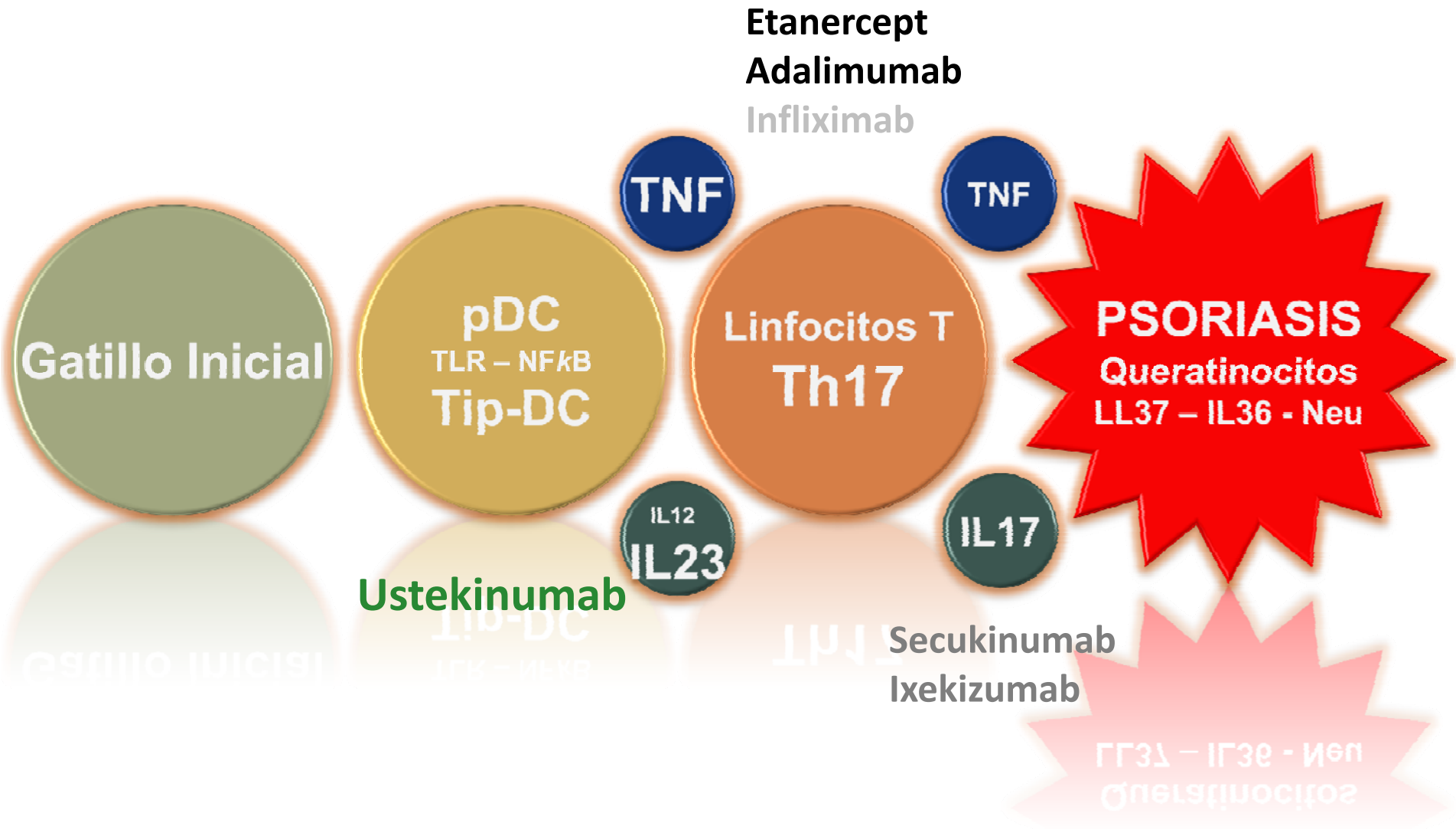
Table 2. Period C Adverse Events[a]

Retreatment:	0.4 mg/kg ADA	0.8 mg/kg ADA		
Randomization:	0.4 mg/kg ADA	0.8 mg/kg ADA	MTX	Total
Patient, n (%)	(n=11)	(n=19)	(n=8)	(n=38)
Any AE	5 (45.5)	14 (73.7)	6 (75.0)	25 (65.8)
Any severe AE	0	2 (10.5)	2 (25.0)	4 (10.5)
Any serious AE	0	0	0	0
Any AE leading to discontinuation	0	0	1 (12.5)	1 (2.6)
Deaths	0	0	0	0
All infections	2 (18.2)	8 (42.1)	4 (50.0)	14 (36.8)
Serious infections	0	0	0	0
Malignancies	0	0	0	0
Allergic reactions	1 (9.1)	0	1 (12.5)	2 (5.3)
Injection-site reactions	0	2 (10.5)	0	2 (5.3)

ADA, adalimumab; AE, adverse event; MTX, methotrexate.

[a]Safety was evaluated in all patients who received≥1 dose of study drug in Period C.

Blancos y biológicos en la psoriasis



Ustekinumab in adolescent patients age 12 to 17 years with moderate-to-severe plaque psoriasis: Results of the randomized phase 3 CADMUS study

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St. Johns, Newfoundland, Canada; Spring House and Philadelphia, Pennsylvania; San Diego, California; Hamburg, Germany; Dallas, Texas; Chicago, Illinois; Bordeaux, France; and Berlin, Germany

Background: Safe and effective therapies are needed for pediatric patients with psoriasis.

Objective: The purpose of this study was to evaluate ustekinumab in patients age 12 to 17 years who had moderate-to-severe psoriasis.

Methods: Patients (n = 110) were randomly assigned to ustekinumab standard dosing (SD; 0.75 mg/kg [≤60 kg], 45 mg [>60-≤100 kg], and 90 mg [>100 kg]) or half-standard dosing (HSD; 0.375 mg/kg [≤60 kg], 22.5 mg [>60-≤100 kg], and 45 mg [>100 kg]) at weeks 0 and 4 and every 12 weeks or placebo at weeks 0 and 4 with crossover to ustekinumab SD or HSD at week 12. Clinical assessments included the proportion of patients achieving a Physician's Global Assessment of cleared/minimal (PGA 0/1), at least 75% improvement in Psoriasis Area and Severity Index (PASI 75), and at least 90% in PASI (PASI 90). Adverse events (AEs) were monitored through week 60.

Results: At week 12, 67.6% and 69.4% of patients receiving ustekinumab HSD and SD, respectively, achieved PGA 0/1 versus 5.4% for placebo ($P < .001$). Significantly greater proportions receiving

J Am Acad Dermatol 2015;73:594-603.

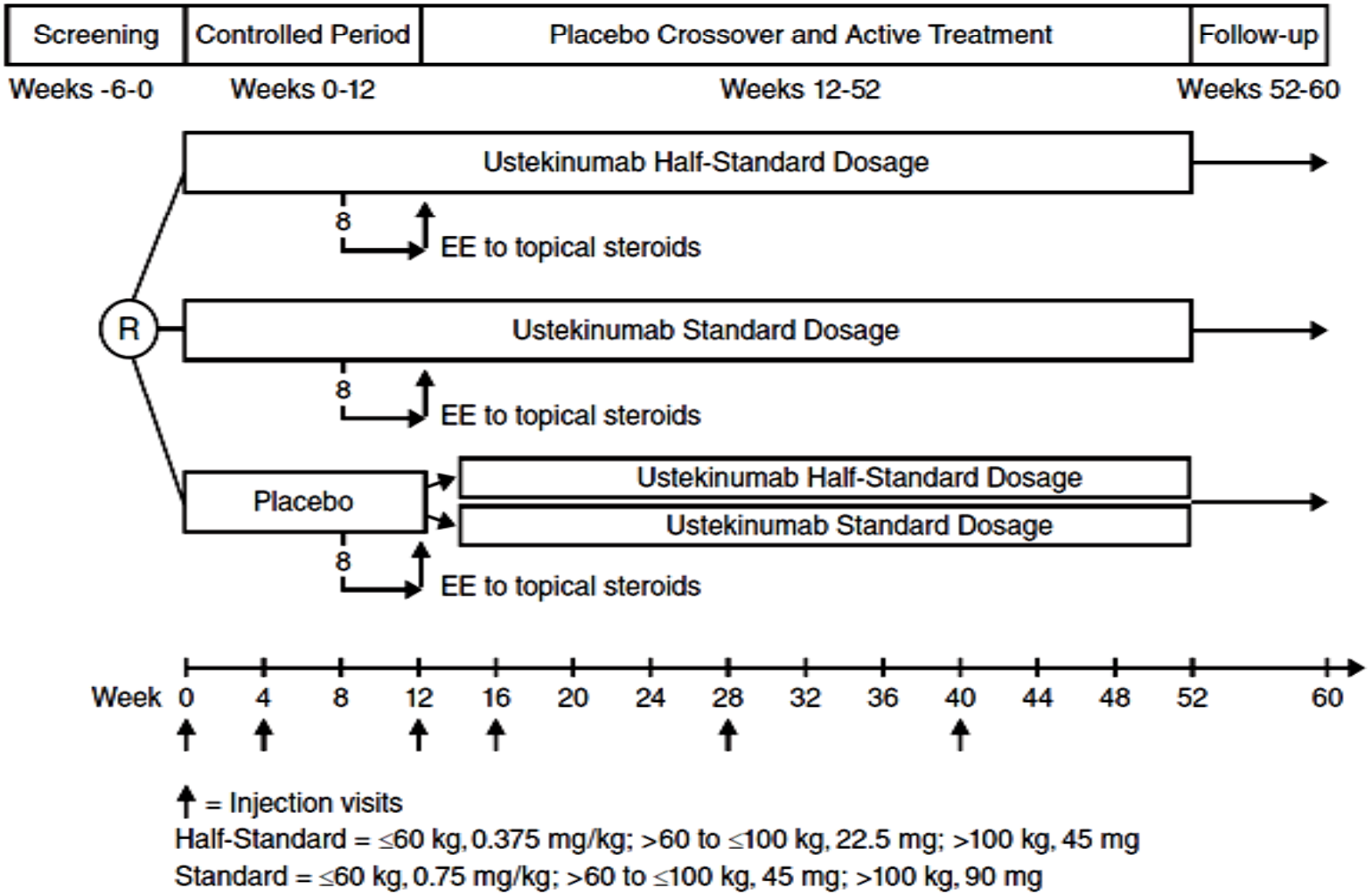
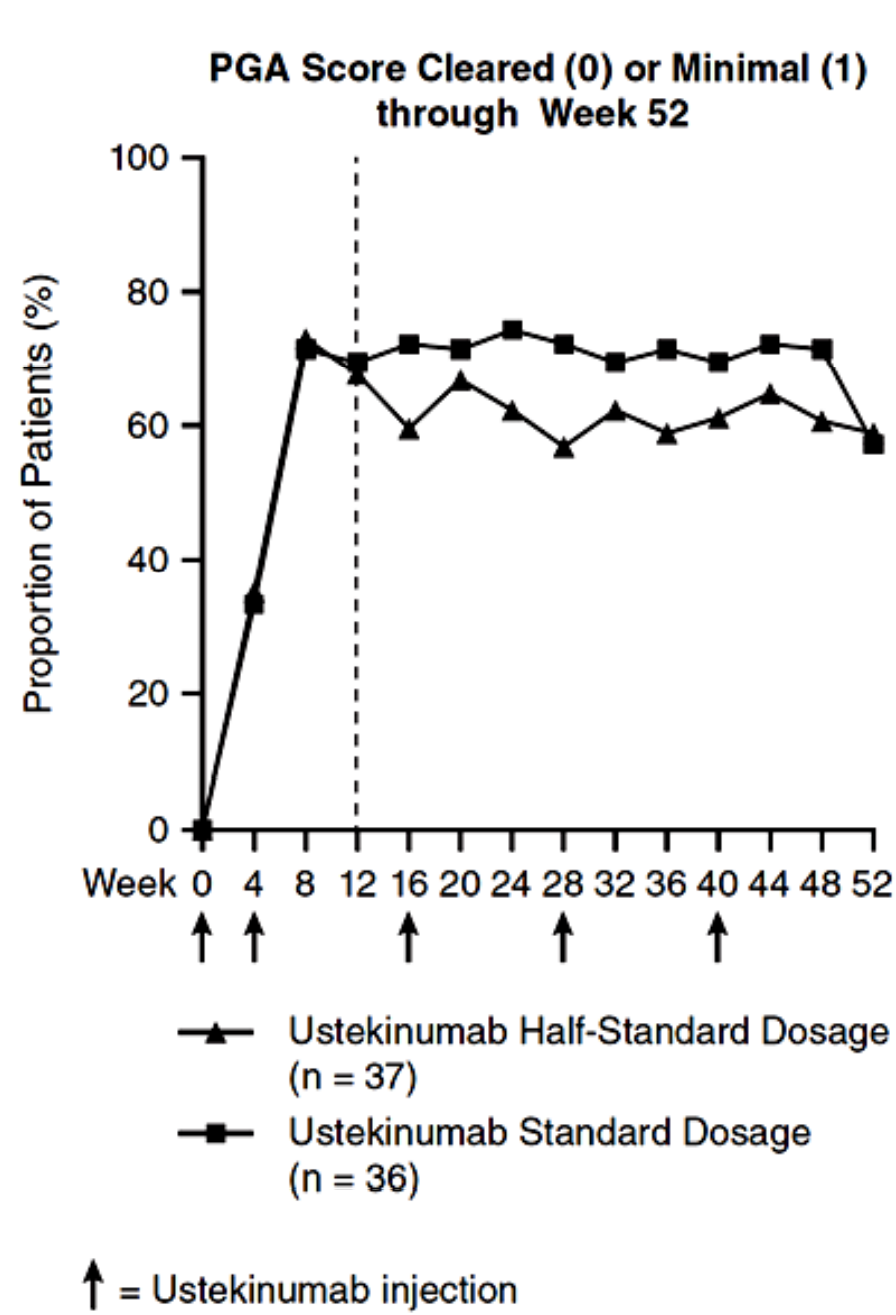
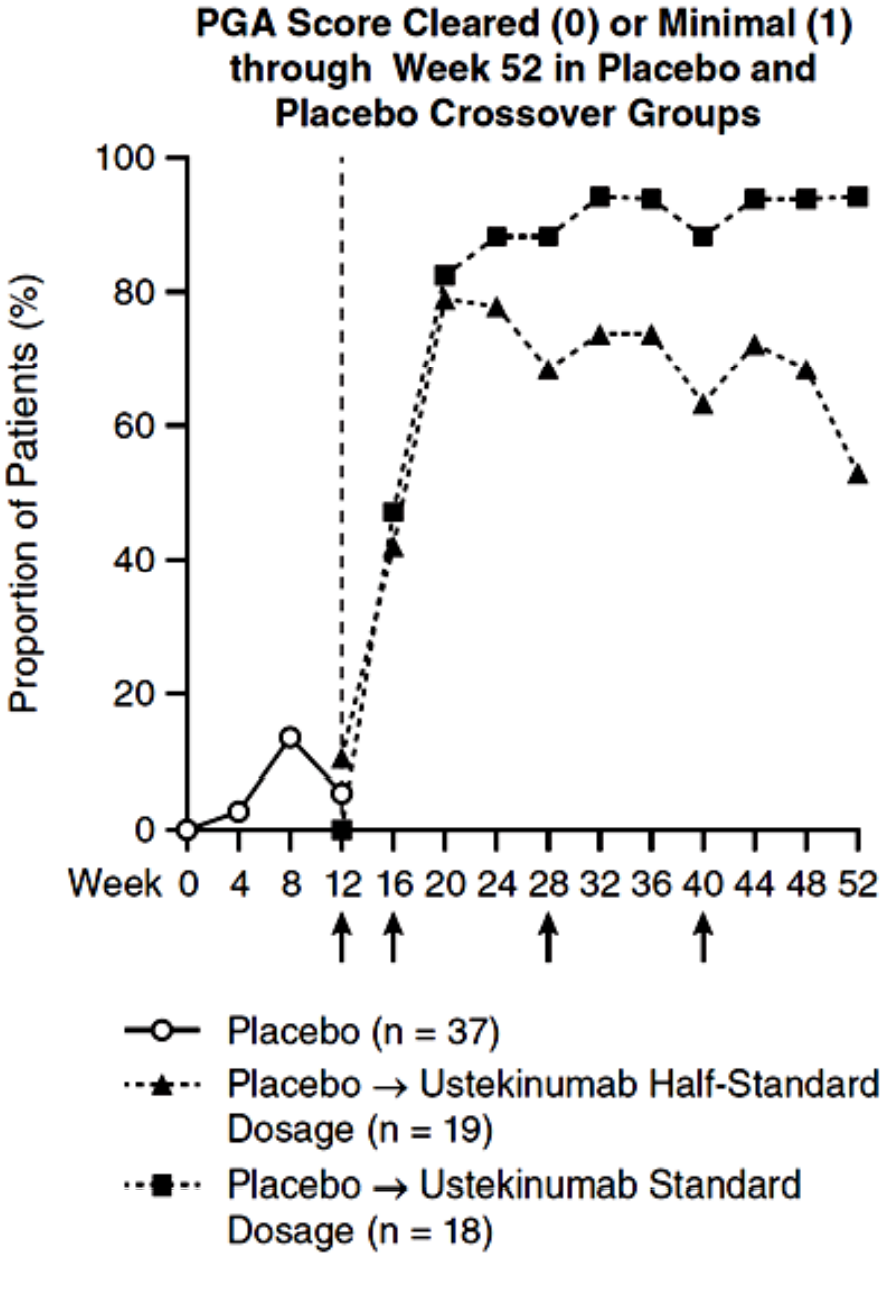


Fig 1. Ustekinumab in adolescent patients with psoriasis. Study schema through week 60. *EE*, Early escape; *R*, randomization.





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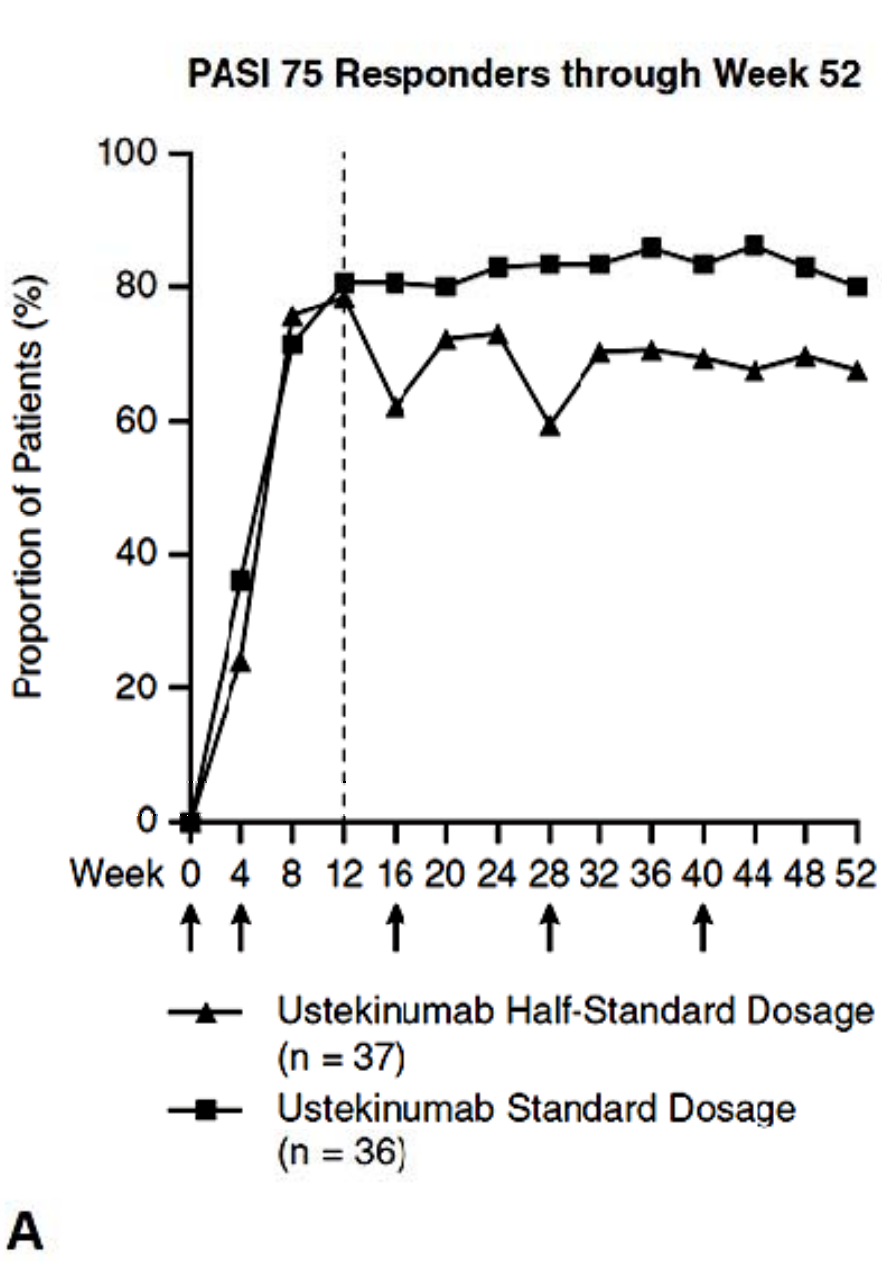

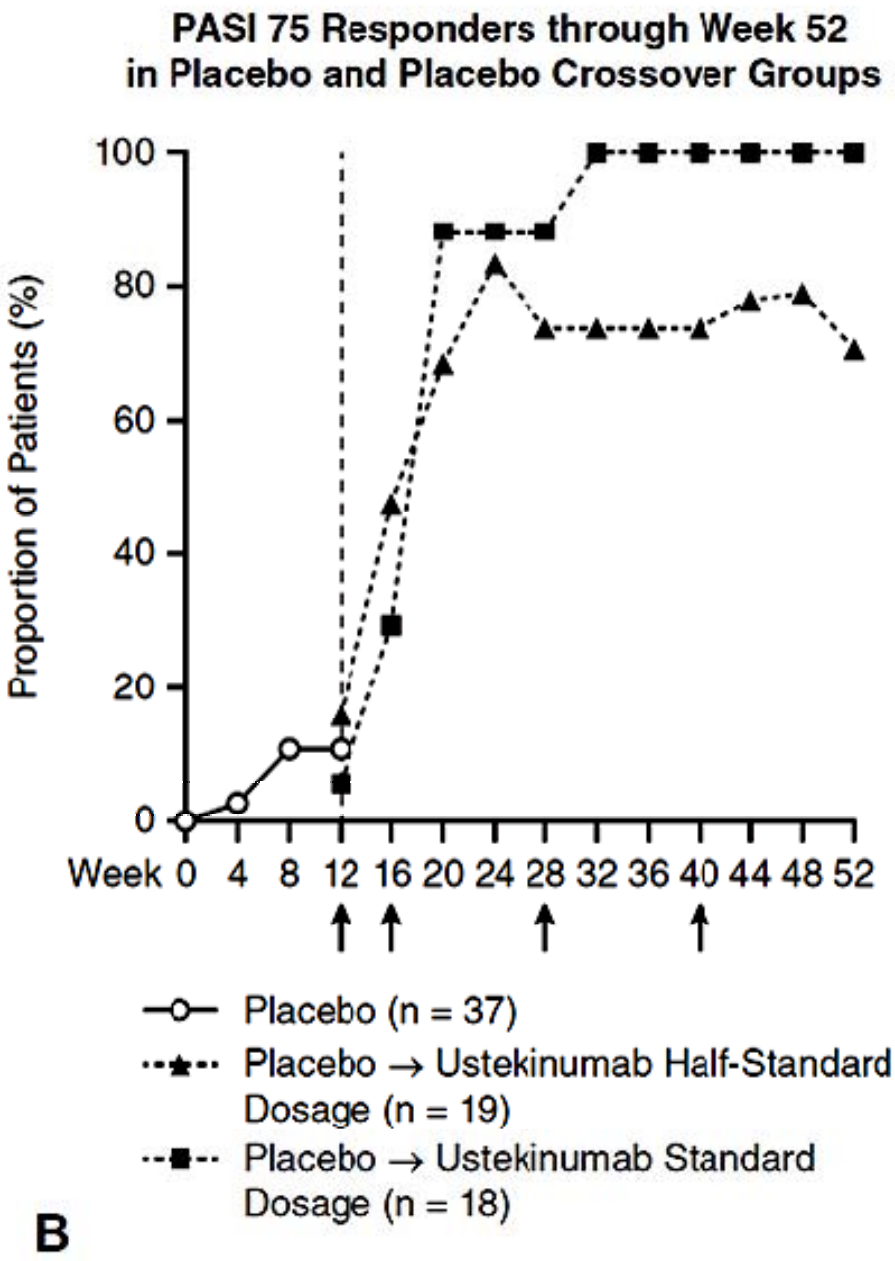

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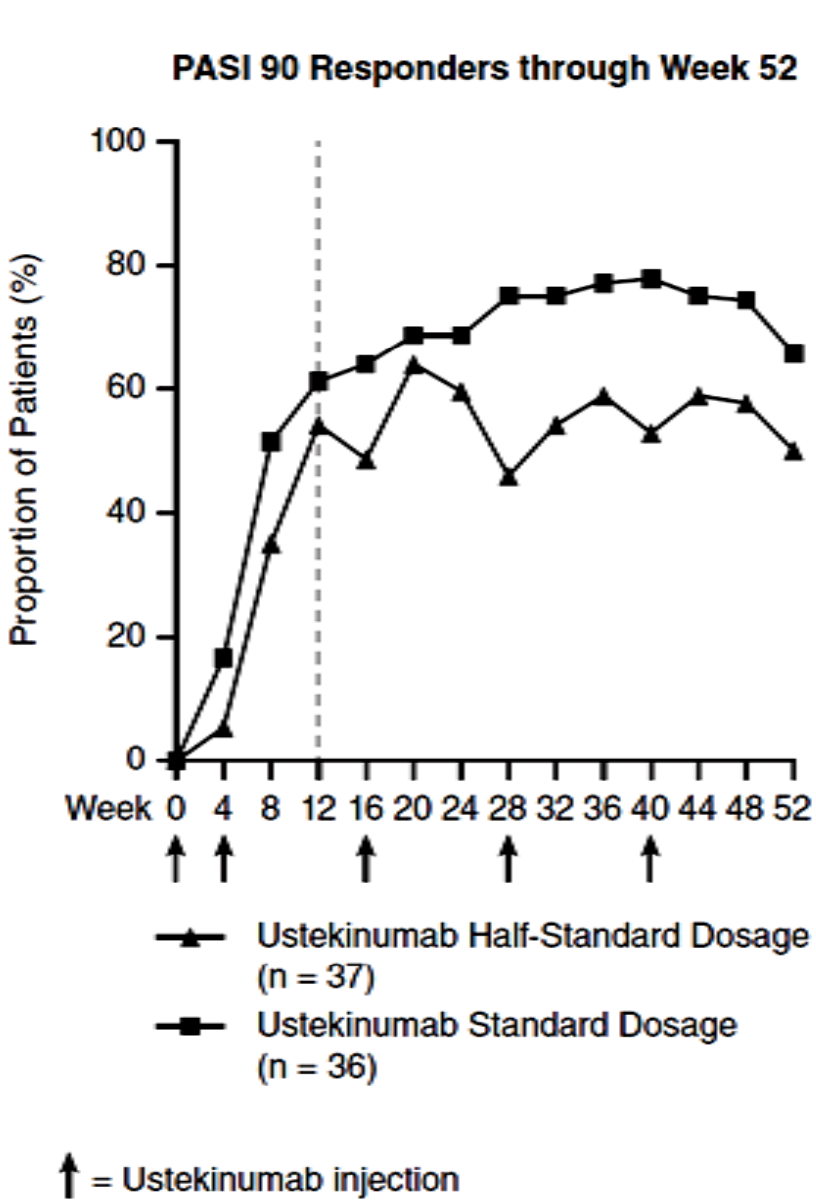

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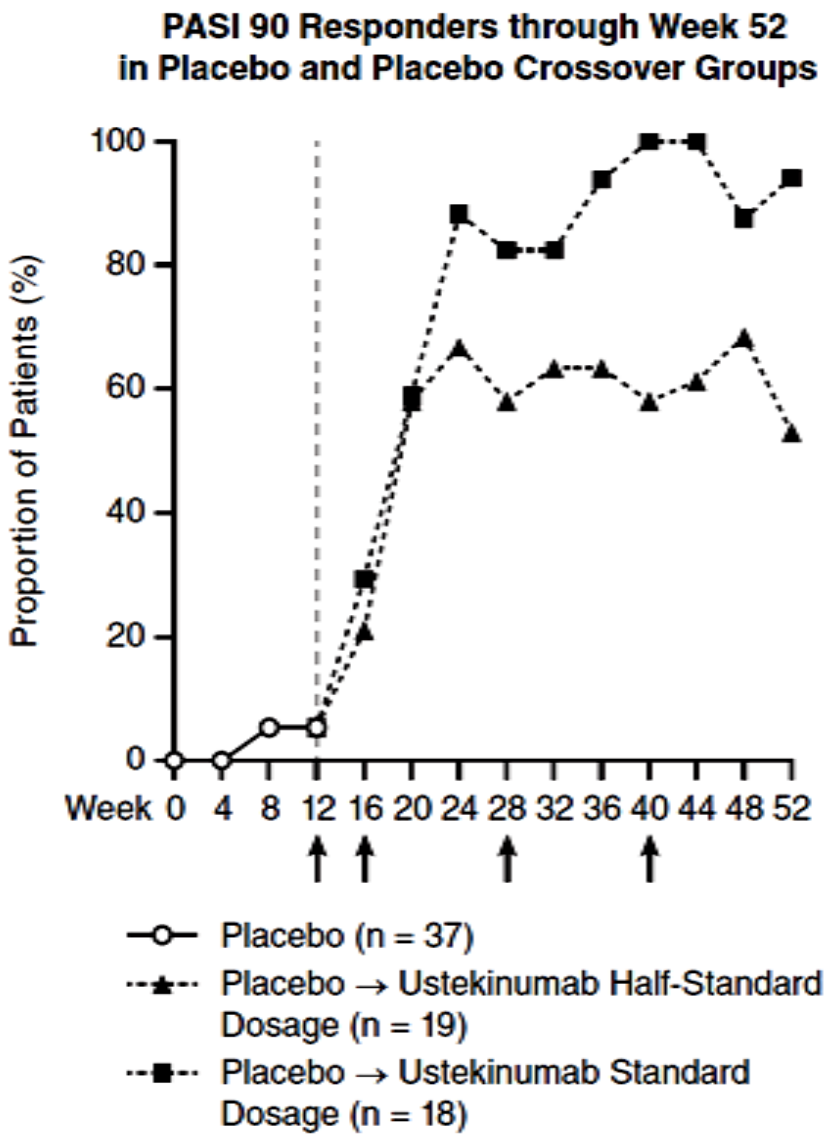

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Adverse events through week 12 (placebo-controlled period)

		Ustekinumab		
	Placebo	Half-standard dosage	Standard dosage	Combined
Patients, n	37	37	36	73
Mean duration of follow-up, wk	12.2	12.2	12.4	12.3
Mean exposure, wk	4.2	4.2	4.1	4.1
Patients with ≥1 AE	21 (56.8)	19 (51.4)	16 (44.4)	35 (47.9)
Patients who discontinued due to AE	0	0	0	0
Infections	14 (37.8)	12 (32.4)	8 (22.2)	20 (27.4)
Patients with ≥1 SAE	0	1 (2.7)	0	1 (1.4)
Serious infections	0	0	0	0
Malignancies	0	0	0	0

Adverse events through week 60

	Ustekinumab				
	Placebo → Half-standard dosage	Placebo → Standard dosage	Half-standard dosage	Standard dosage	Combined
Patients, n	19	18	37	36	110
Mean duration of follow-up, wk	45.9	46.9	55.2	58.0	53.2
Mean exposure, wk	27.3	28.1	38.0	39.0	34.9
Patients with ≥1 AE	15 (78.9)	13 (72.2)	33 (89.2)	29 (80.6)	90 (81.8)
Patients who discontinued due to AE	2 (10.5)	0	2 (5.4)	0	4 (3.6)
Infections	13 (68.4)	11 (61.1)	26 (70.3)	24 (66.7)	74 (67.3)
Patients with ≥ 1 SAE	0	0	5 (13.5)	1 (2.8)	6 (5.5)
Serious infections	0	0	1 (2.7)	1 (2.8)	2 (1.8)
Malignancies	0	0	0	0	0

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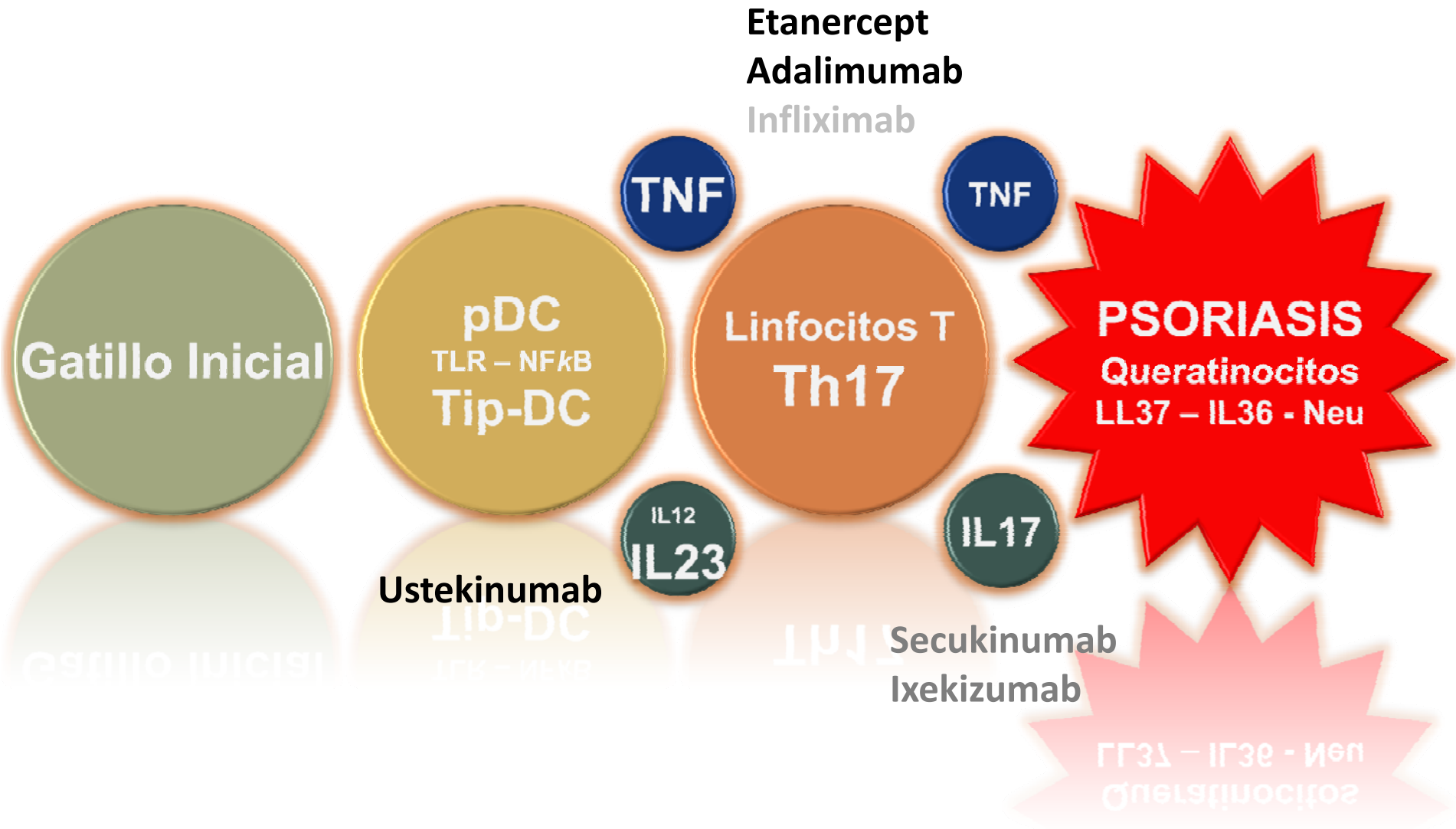
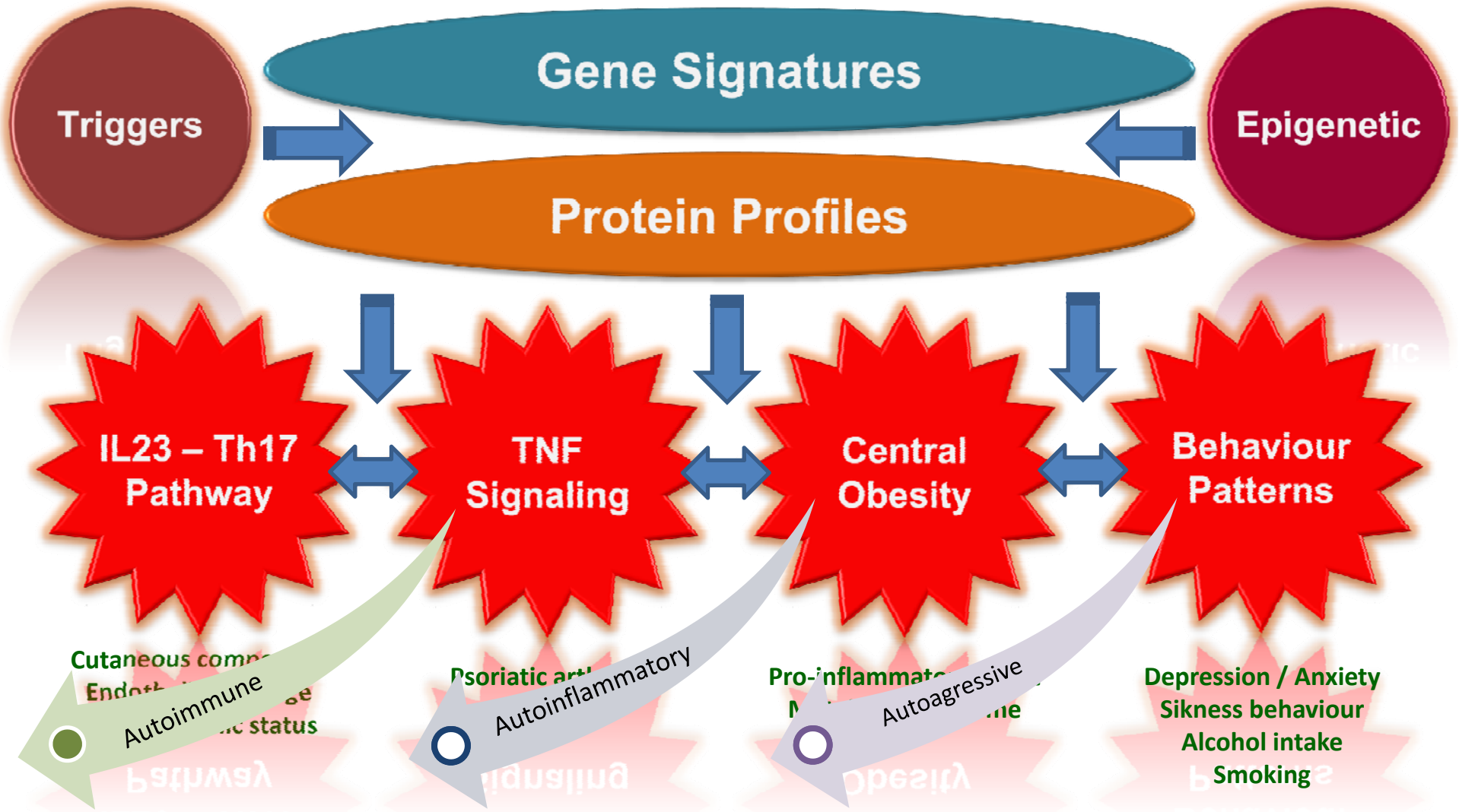



Treat-to-target

Treat-to-target

- Compromisos focales
  - Visible
  - Palmo-plantar
  - Genital
- Síntomas particulares
  - Prurito
  - Descamación
- Evaluaciones indirectas
  - Rendimiento escolar
  - Productividad laboral


Triggers
Gene Signatures
Protein Profiles
Epigenetic
IL23 – Th17 Pathway
TNF Signaling
Central Obesity
Behaviour Patterns
Autoimmune
Autoinflammatory
Autoagressive
Depression / Anxiety
Sikness behaviour
Alcohol intake
Smoking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