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Early Treatment for Alopecia Areata Prevention (ETAAP)

Matthew Harries

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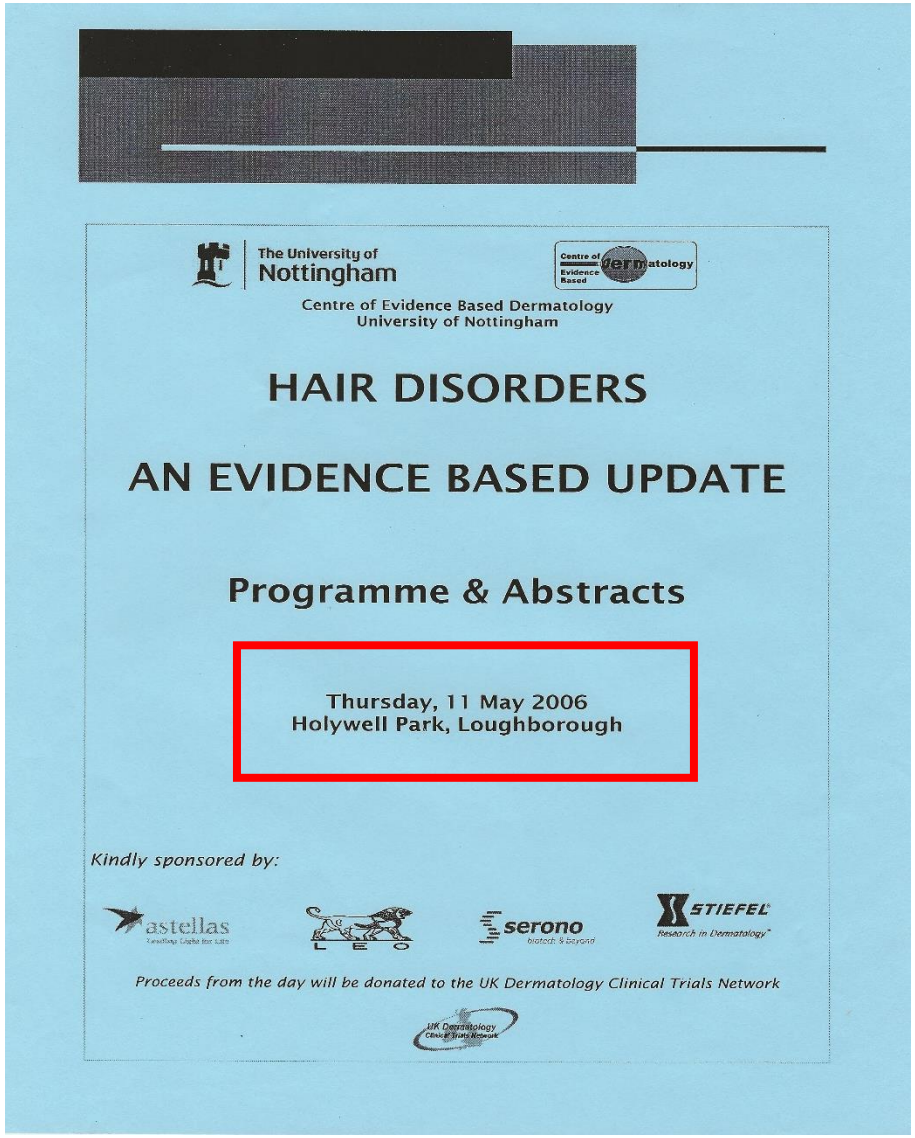
The University of Manchester
Salford Royal NHS Foundation Trust
Manchester
UK

EBM Hair Update 15th May 2019

Good to be Back [1]!

Good to be Back [2]!



The University of Nottingham

Centre of Evidence Based Dermatology
University of Nottingham

HAIR DISORDERS

AN EVIDENCE BASED UPDATE

Programme & Abstracts

Thursday, 11 May 2006
Holywell Park, Loughborough

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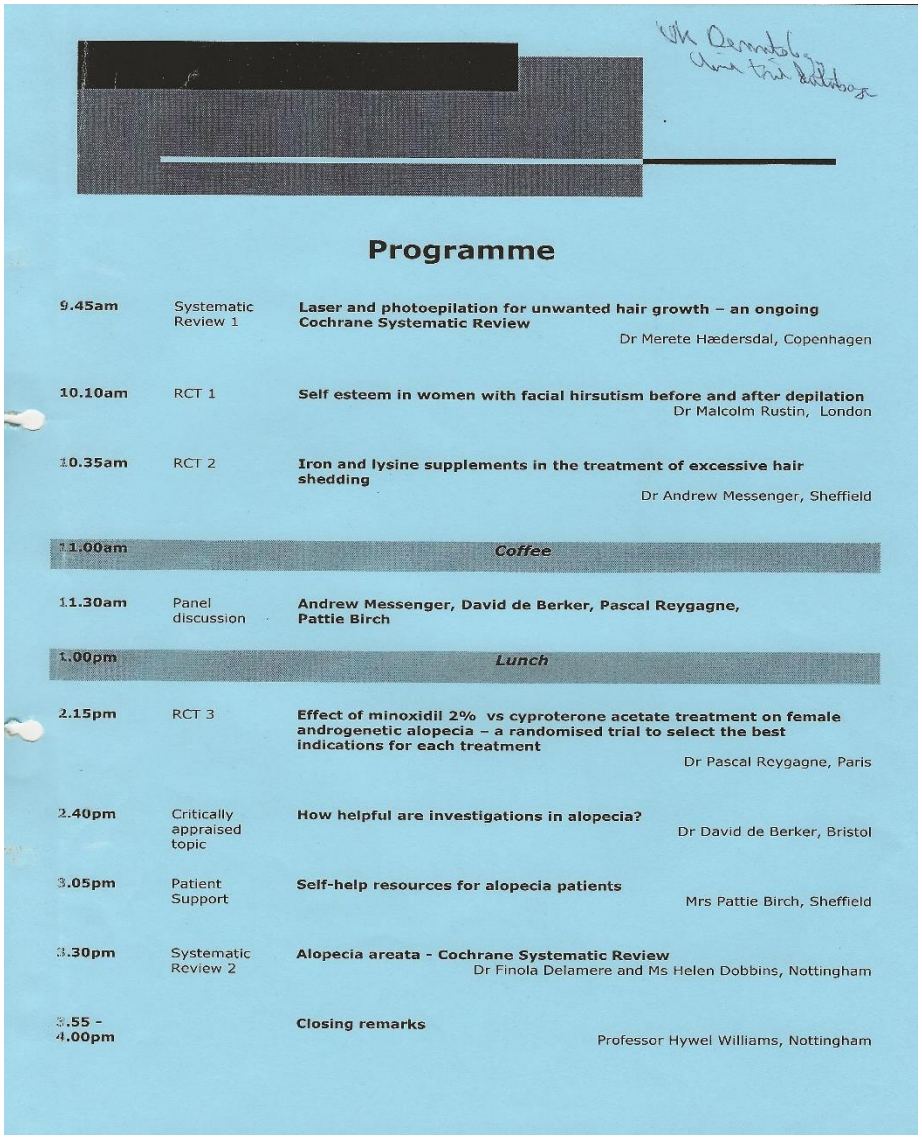
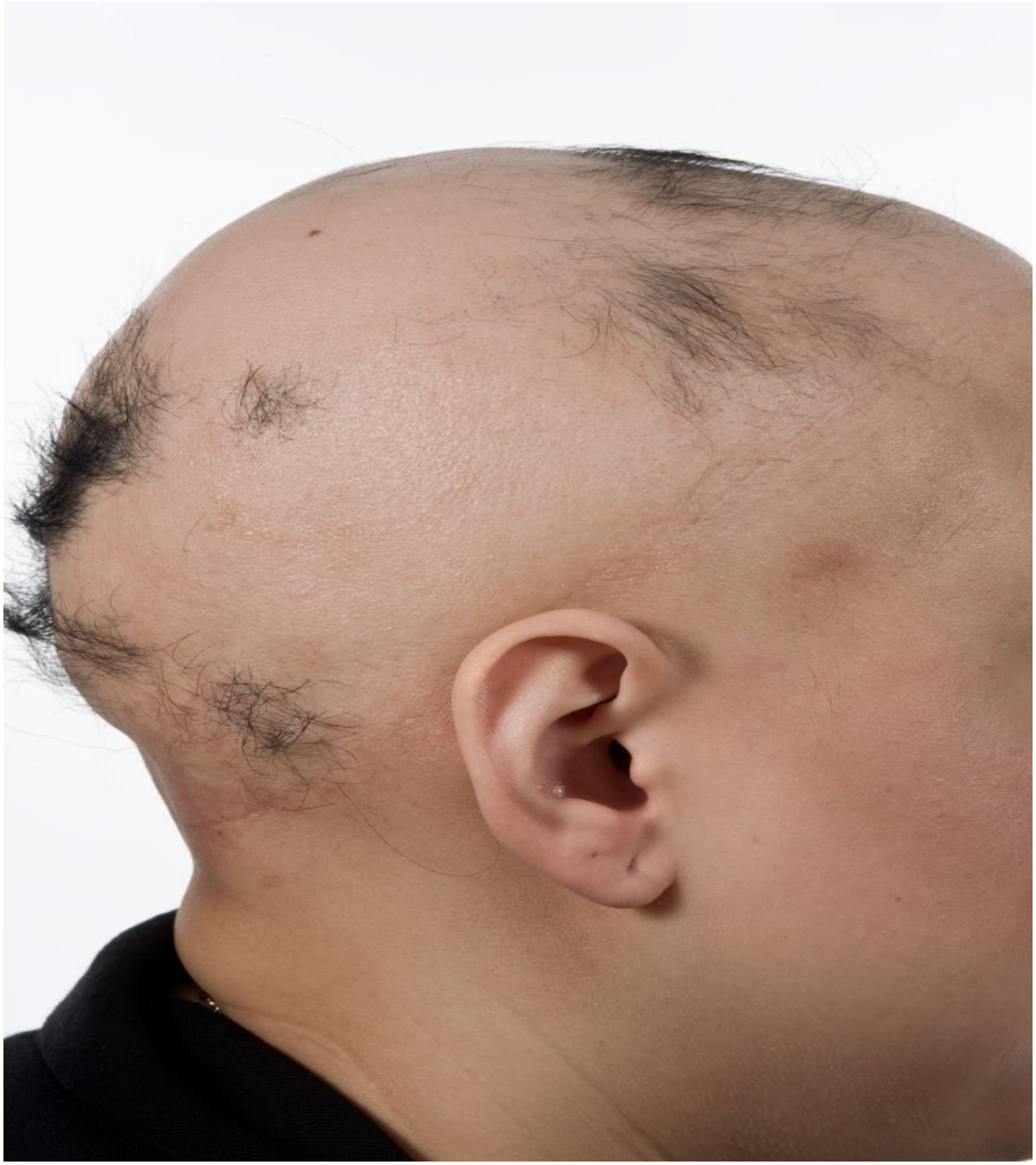
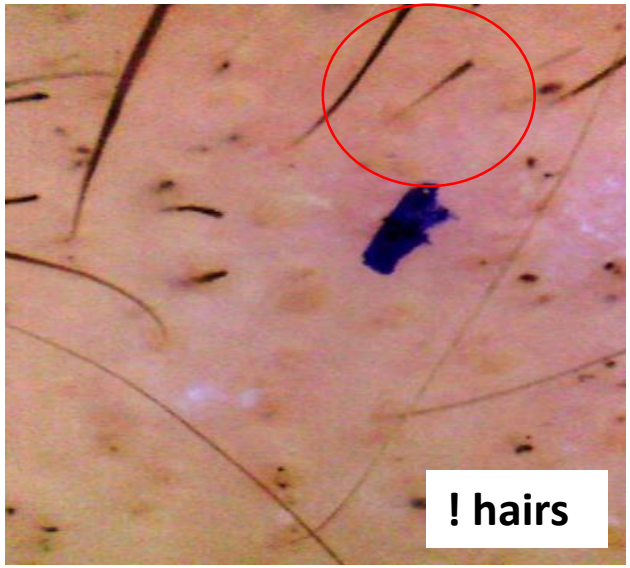
Proceeds from the day will be donated to the UK Dermatology Clinical Trials Network

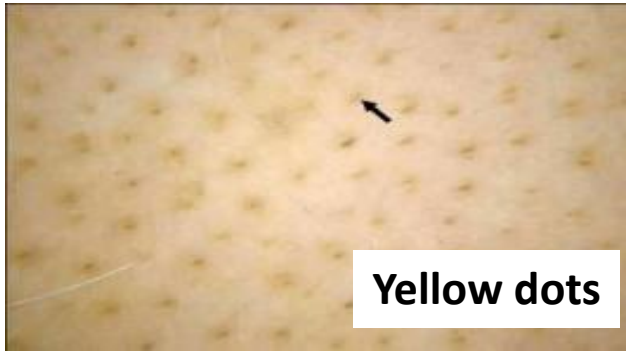


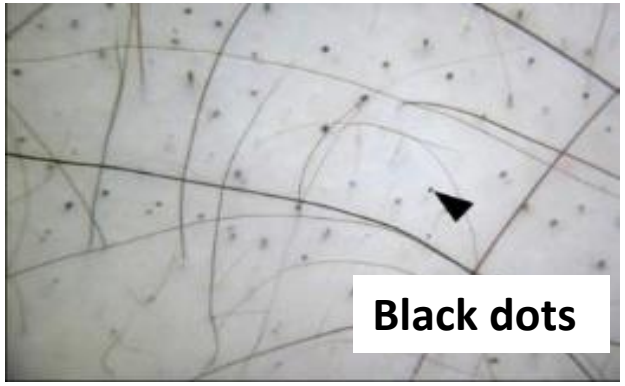
Programme

9.45am	Systematic Review 1	**Laser and photoepilation for unwanted hair growth – an ongoing Cochrane Systematic Review** Dr Merete Hædersdal, Copenhagen
10.10am	RCT 1	**Self esteem in women with facial hirsutism before and after depilation** Dr Malcolm Rustin, London
10.35am	RCT 2	**Iron and lysine supplements in the treatment of excessive hair shedding** Dr Andrew Messenger, Sheffield
11.00am		*Coffee*
11.30am	Panel discussion	**Andrew Messenger, David de Berker, Pascal Reygagne, Pattie Birch**
1.00pm		*Lunch*
2.15pm	RCT 3	**Effect of minoxidil 2% vs cyproterone acetate treatment on female androgenetic alopecia – a randomised trial to select the best indications for each treatment** Dr Pascal Reygagne, Paris
2.40pm	Critically appraised topic	**How helpful are investigations in alopecia?** Dr David de Berker, Bristol
3.05pm	Patient Support	**Self-help resources for alopecia patients** Mrs Pattie Birch, Sheffield
3.30pm	Systematic Review 2	**Alopecia areata - Cochrane Systematic Review** Dr Finola Delamere and Ms Helen Dobbins, Nottingham
3.55 - 4.00pm		**Closing remarks** Professor Hywel Williams, Nottingham




! hairs


Yellow dots


Black dots

GUIDELINES

BJD
British Journal of Dermatology

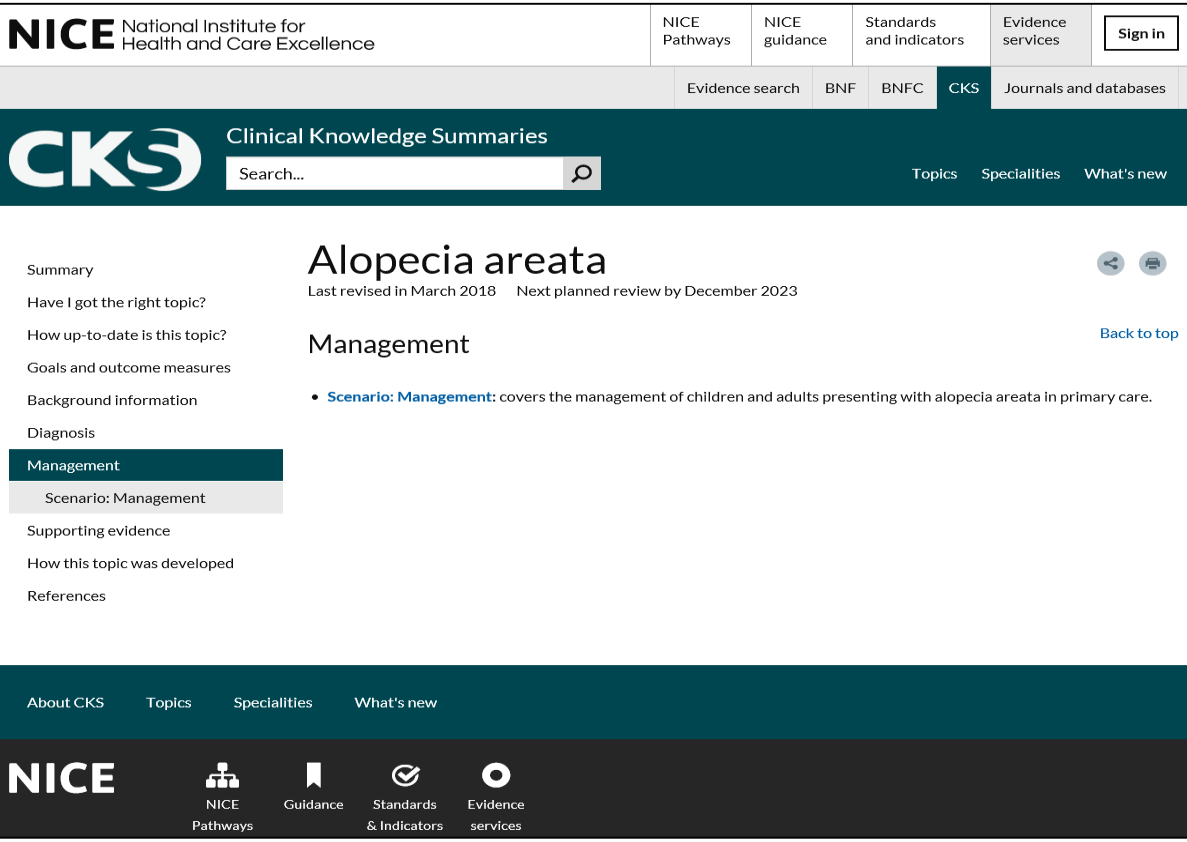
British Association of Dermatologists' guidelines for the management of alopecia areata 2012

A.G. Messenger, J. McKillop,* P. Farrant,† A.J. McDonagh and M. Sladden‡

Department of Dermatology, Royal Hallamshire Hospital, Sheffield S10 2JF, U.K.
*Alopecia UK, 5 Titchwell Road, London SW18 3LW, U.K.
†Department of Dermatology, Brighton General Hospital, Elm Grove, Brighton BN2 3EW, U.K.
‡Department of Medicine, University of Tasmania, Hobart, Australia

"Leaving alopecia areata untreated is a legitimate option for many patients"

"Spontaneous remission occurs in up to 80% of patients with limited patchy hair loss of short duration (< 1 year)."



"If there is no hair regrowth and there is *less than* 50% hair loss, discuss the option of watchful waiting with no current treatment needed"

Clinical presentation	Proportion with spontaneous regrowth	Risk of developing chronic AA	Risk of developing AT or AU
Solitary stable patch of AA ≤6 months duration	87%	13%	6%
Solitary stable patch of AA ≥6 months but ≤12 months	35%	65%	30%
Solitary stable patch of AA ≥12 months duration	0	100%	45%
Multiple patches within 6 months of initial presentation	65%	35%	15%
Aged 0–6 years at initial presentation	0	100%	45%
Aged 6–12 years at initial presentation	60%	40%	18%

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis.

Ikeda T. A new classification of alopecia areata. *Dermatology* 1965; 131: 421–45.

Alopecia areata: A long term follow-up study of 191 patients

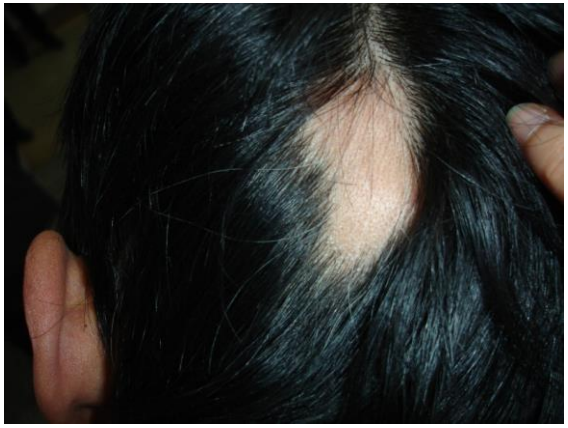
Antonella Tosti, MD, Sara Bellavista, MD, and Matilde Iorizzo, MD
Bologna, Italy

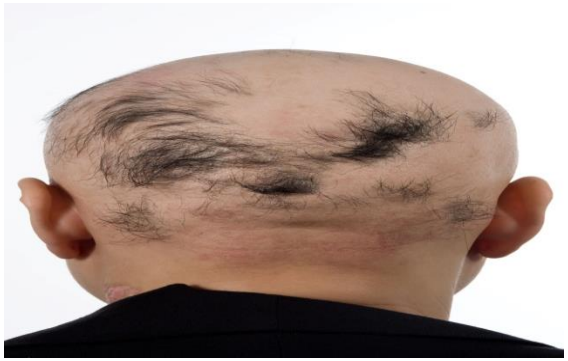
- Contacted 16-23 years later
- Significant tendency for AA to worsen with time
  - **19%** with mild disease (<50% area) had **AT / AU** at follow-up
  - **93%** with AU still had extensive disease (**AT / AU**) at follow-up
  - **3%** with extensive disease (AT / AU) were **disease free** at follow-up

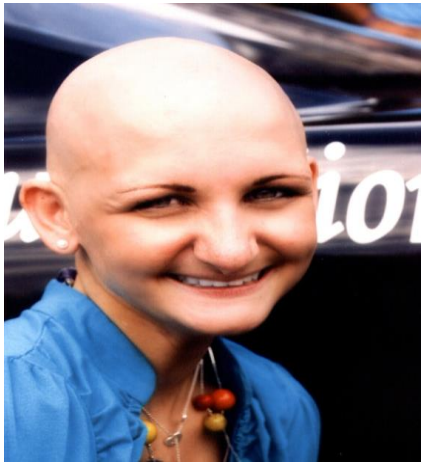
(J Am Acad Dermatol 2006;55:438-41.)

Poor Prognosis in AA

- Extensive disease
- Long disease duration
- Onset before puberty
- Atopy
- Associated autoimmune disease
- Nail disease
- Positive FH

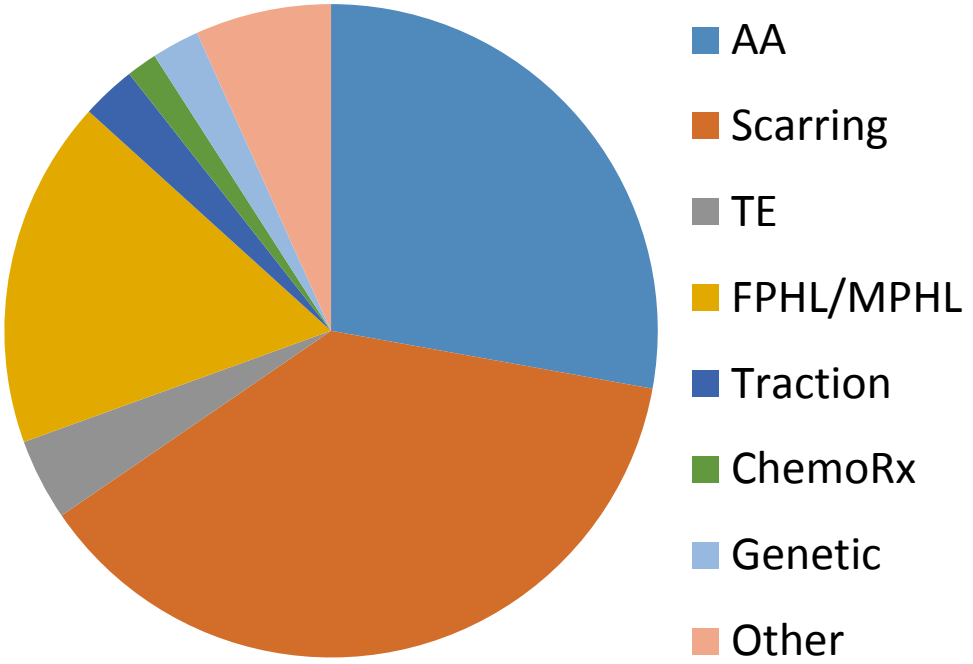






SRFT Hair Clinic

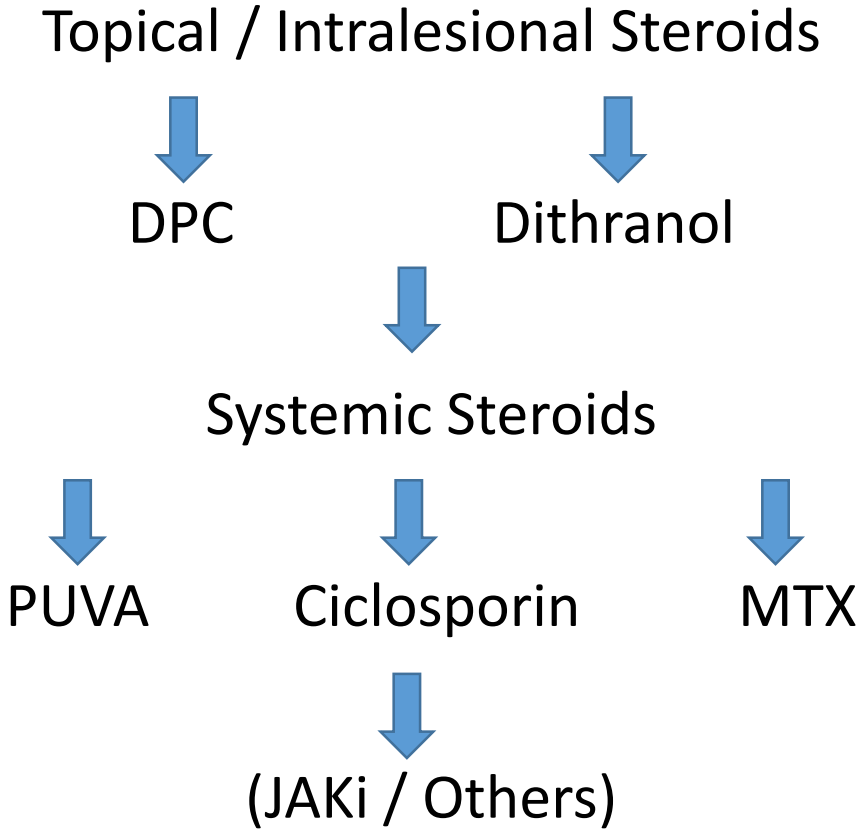
(2013 – present)
[n=1883]



522 AA pts with >30 % AT/AU

Impact on the NHS

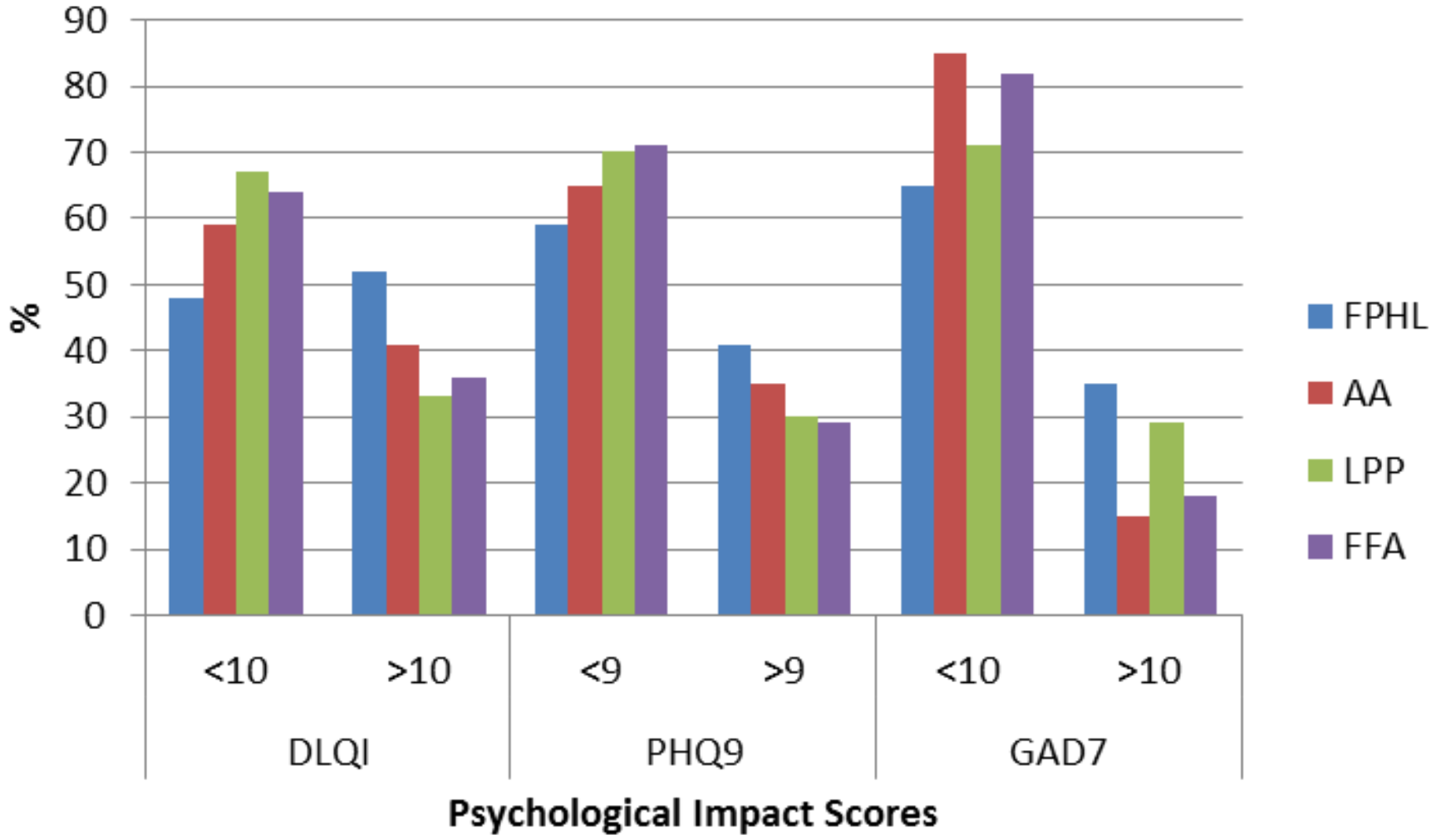
STANDARD TREATMENT PATHWAY



- Multiple unsuccessful treatments
  - Clinic visits
  - Treatment / monitoring costs
- Estimated cost for DPC + wig treatment in Glasgow = £1500 per patient / year

(Phillips R, Holmes S. WCHR Abstract 2019)

Significant Psychological Impact



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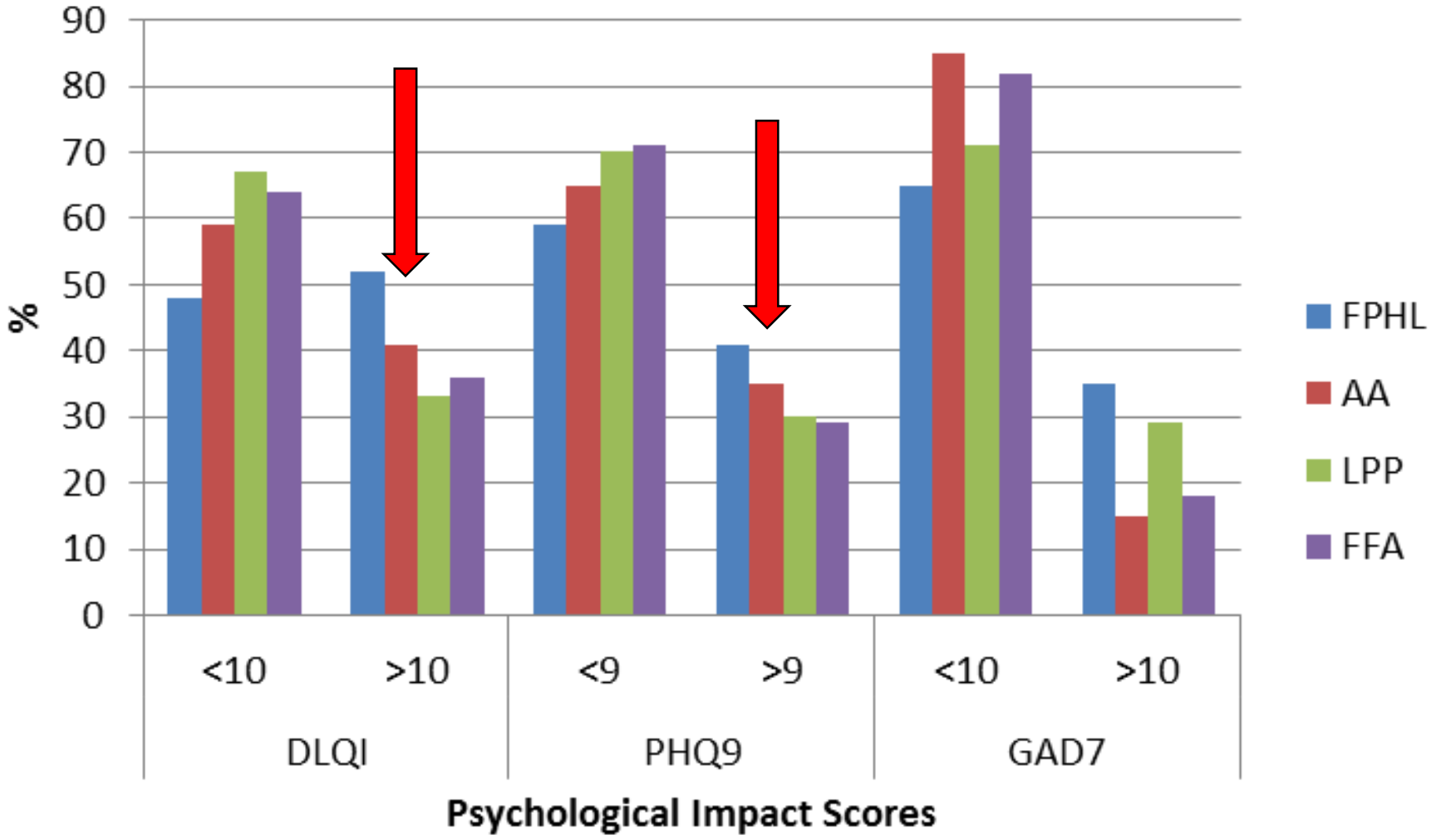

Alopecia Areata Priority Setting Partnership (PSP)

Rank	Uncertainty
1	What are the causes of alopecia areata? For example, medications, medical problems, lifestyle, vaccinations
2	Are immunosuppressant therapies (e.g. methotrexate; mycophenolate mofitil) better than placebo in the treatment of alopecia areata?
3	In alopecia areata, are biological therapies (including janus kinase (JAK) inhibitors and anti-cytokine therapies) more effective than placebo in causing hair regrowth?
4	Are psychological interventions helpful in alopecia areata?
5	Can progression of alopecia areata be prevented by early diagnosis and treatment?
6	Do certain foods, vitamins or nutritional supplements improve hair regrowth in alopecia areata?
7	What can be learnt about alopecia areata from other autoimmune conditions?
8	In whom does alopecia areata hair loss progress and why?
9	Do any treatments have a long-term therapeutic benefit in alopecia areata?
10	How effective are alternative therapies in alopecia areata?

(MacBeth et al. Br J Dermatol 2017)

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(MacBeth et al. Br J Dermatol 2017)

Lessons from other Immune-Mediated Inflammatory Disorders (IMID)

Aggressive early intervention in RA, Crohn's disease & MS:

Reduce tissue damage and longer-term complications

Induces disease-free remission

(Girolomoni et al. J Dermatol Treat 2015)

Is there any Evidence that Early Treatment effects Prognosis in AA?

Interventions for alopecia areata (Review)

Delamere FM, Sladden MJ, Dobbins HM, Leonardi-Bee J

THE COCHRANE COLLABORATION®

"There is no good trial evidence that any treatment provide long-term benefit to patients with alopecia areata, alopecia totalis and alopecia universalis."

2008

Clinical Observation: Better Outcomes with Early Treatment?

- 68 Pt with chronic AA treated with systemic therapy and followed for 2-7 years
- Rates of AT/AU = 17.6% [Expected rate 45% based on Ikeda data]
- Rationale to treat chronic AA to prevent AT/AU

(Cranwell et al. Aus J Dermatol 2018)

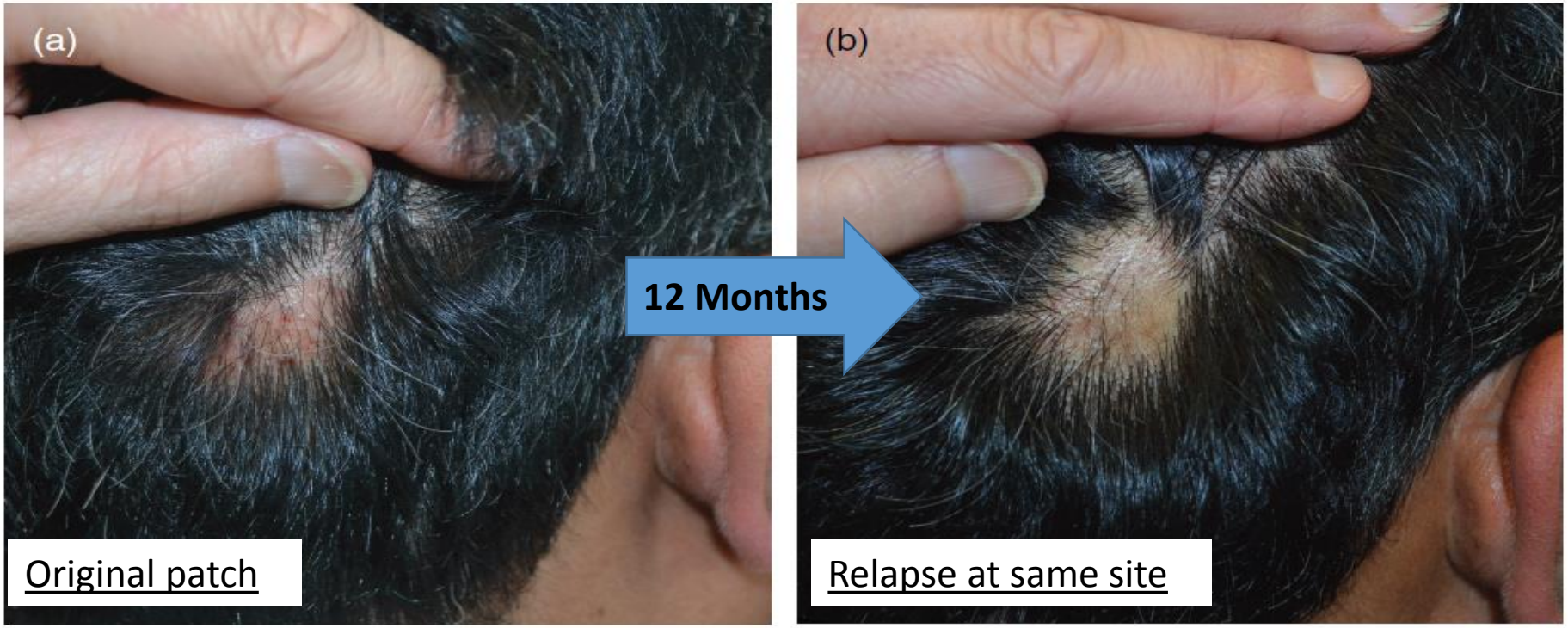
- Shorter duration between disease onset and treatment commencement
- “good” prognosis in children <10yrs old with “early onset” AA

(Suh et al. Ann Dermatol 2014)

- Treatment with pulsed systemic corticosteroids for extensive AA
- more effective, and less likely to relapse, when started within 1 year of disease onset compared with treatments commenced later on

(Yang et al. Ann Dermatol 2013)

Clinical Observation: AA Recurring at Previously Affected Sites



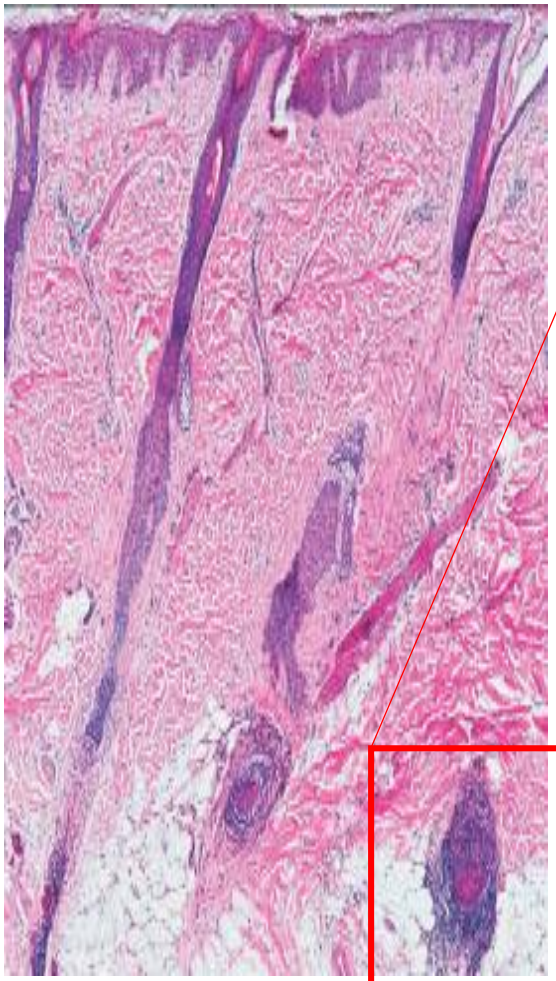
If previously affected skin is more susceptible to future attack = Argues for aggressive early treatment to prevent more extensive scalp involvement

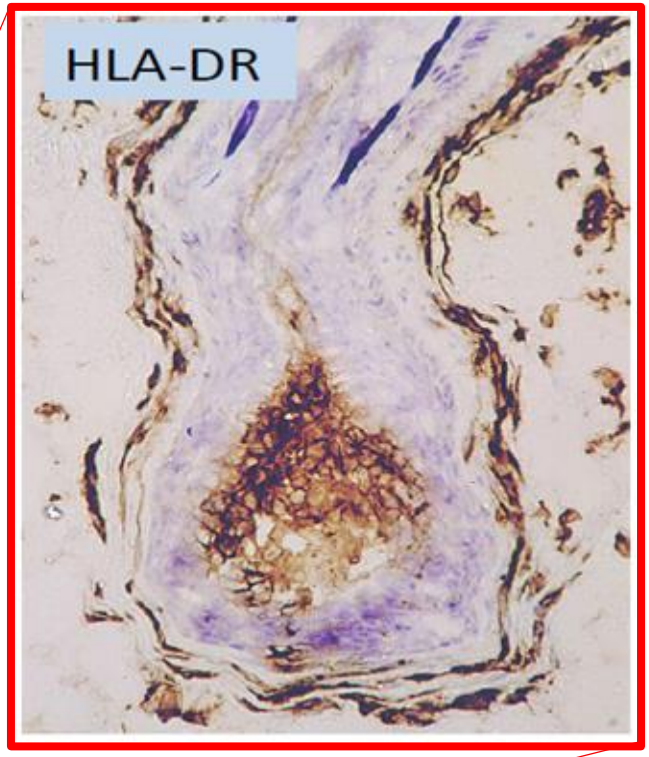
(Li & Sinclair. Aus J Dermatol 2016)

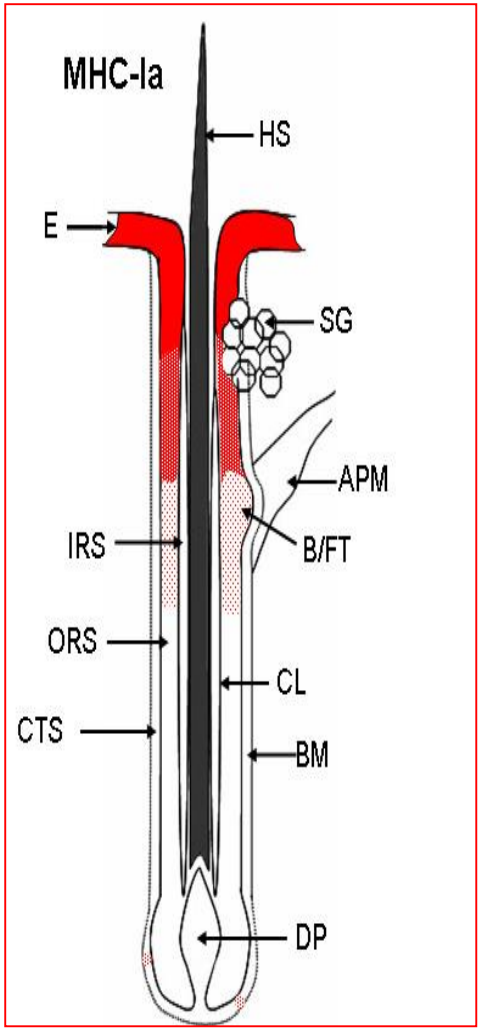
Is there Any Biological Rationale for Early Treatment?

As there is no tissue damage in AA

Alopecia Areata – Bulb IP Collapse



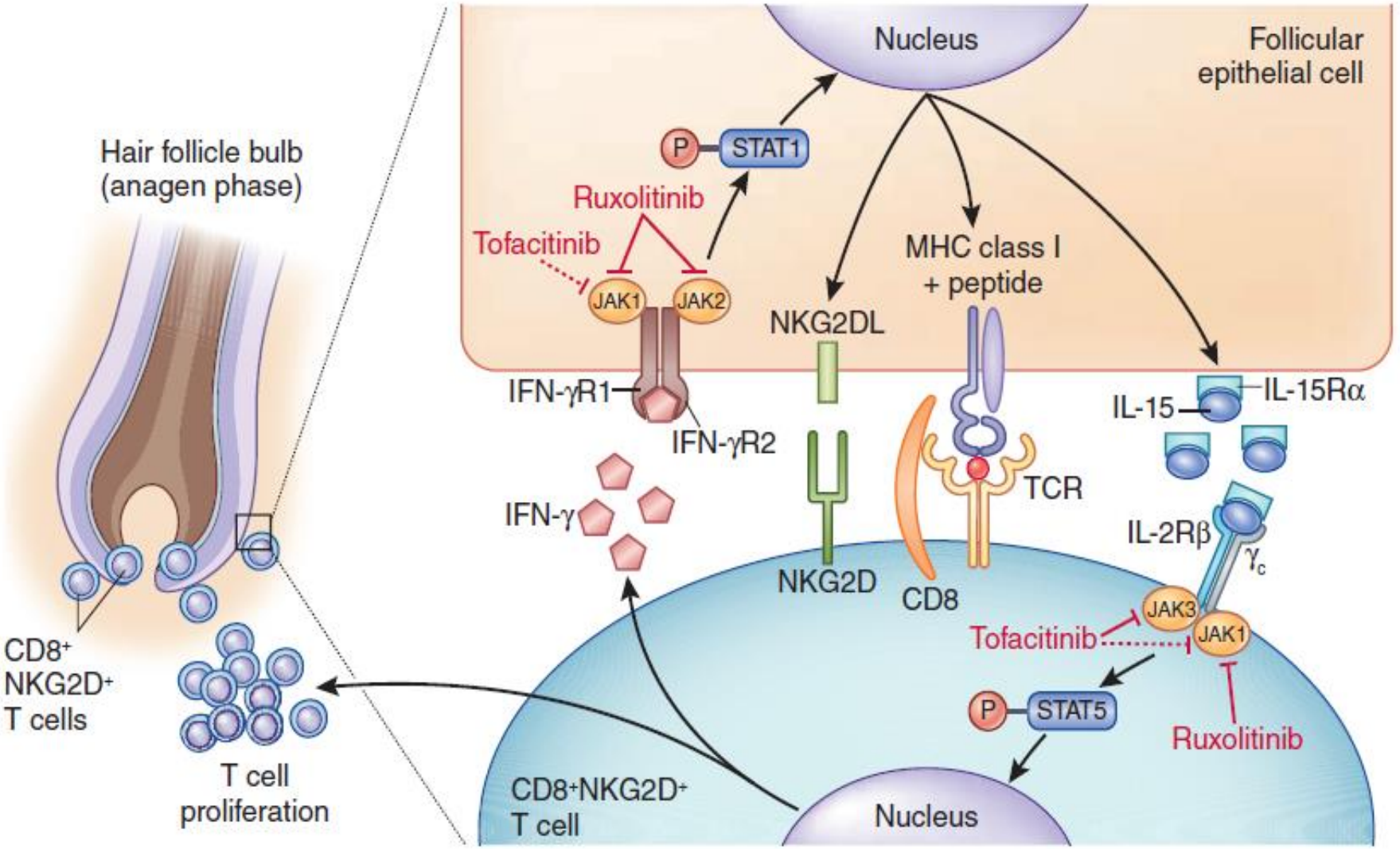




AA

Normal

Positive feedback loop in AA



(From Divito and Kupper. *Nat Med* 2014)

As has been proposed in Psoriasis, it is conceivable that stimulation of a small region of AA-predisposed skin results in an immune reaction that leads to the development of lesions at local and distant body sites

(Girolomoni et al. J Dermatol Treat 2015)

- Disease recrudesce in susceptible tissue
  - Ongoing immune dysfunction / Sub-clinical inflammation?
  - Incomplete IP restoration?
  - “Molecular scar”

  (Girolomoni et al. J Dermatol Treat 2015)

Testing the Hypothesis

Early treatment can prevent disease progression in AA

A Successful Early Treatment Strategy in AA would:

- Target those most likely to benefit from early treatment
- Improve Q of L & Reduce social stigmatisation
- Modify the disease course
  - Achieving prolonged medication-free remission
- Cost-effective management strategies

Early Treatment for Alopecia Areata Prevention (ETAAP)

Possible Trial Design….

"Classic"

Single intervention vs. placebo given early in disease course

"Pragmatic"

Early intervention (of whatever type) vs. deferred treatment

Early Treatment for Alopecia Areata Prevention (ETAAP)

Feasibility work…

- Target population and barriers to recruitment
  - Early case identification
  - Acceptability of interventions
- Preferred outcome measures
- Power calculation
- Potential economic impact

Early Treatment for Alopecia Areata Prevention (ETAAP)

Feasibility work…

- Target population and barriers to recruitment
  - ➢Early case identification
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Engagement with Primary Care
Surveys
Focus group work
Statistics Advice

…eventually Leading to a Clinical Trial

ETAAP: Progress

- Building the Team
  - Dermatologists / Patient / GPwSI / (Qualitative researcher) / Statistician
- Seeking advice
  - University of Manchester Primary Care Academic Unit
  - NIHR Research Design Service (RDS)
  - UK-DCTN
- Secured Funding
  - Alopecia UK
- Ethics
  - NIHR Portfolio adoption
- PUBLISH RESULTS

EHRS 2020

18th-20th June 2020, Sheffield, UK

19TH EUROPEAN HAIR RESEARCH SOCIETY MEETING

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Save the Date

18th - 20th June 2020

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alopecia uk

Abby MacBeth, Andrew Messenger,
Susan Holmes, Leila Asfour, Calvin Heald

UK Dermatology Clinical Trials Network