

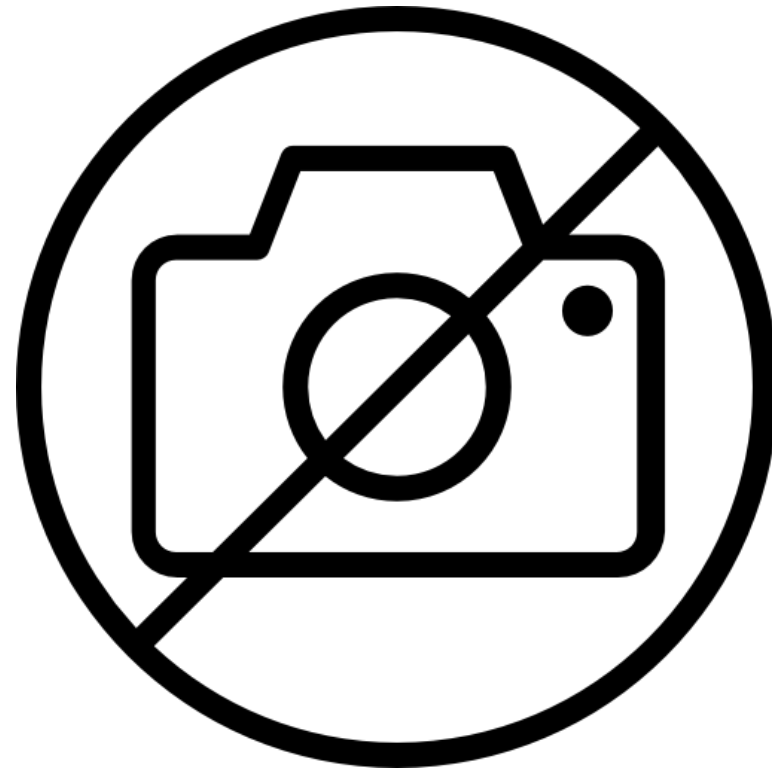
# Ontwikkelingen in de behandeling van Alopecia areata

DirkJan Hijnen



# Disclosures

- Register voor AA, sponsoring van Pfizer en onderhandelingen met Lilly
- Onderzoek naar eczeem in samenwerking met diverse farmaceuten (Astra Zeneca, Almirall, Galderma, LEO pharma, Abbvie, Sanofi, UCB)



# Eczeem + AA & JAK remmer

**8/2019**

**5/2021**

**8/2022**

# Behandeling van alopecia areata

- Lokale behandeling(en)
- Systemische behandeling(en)
  - 'klassieke middelen'
  - nieuwe behandelingen

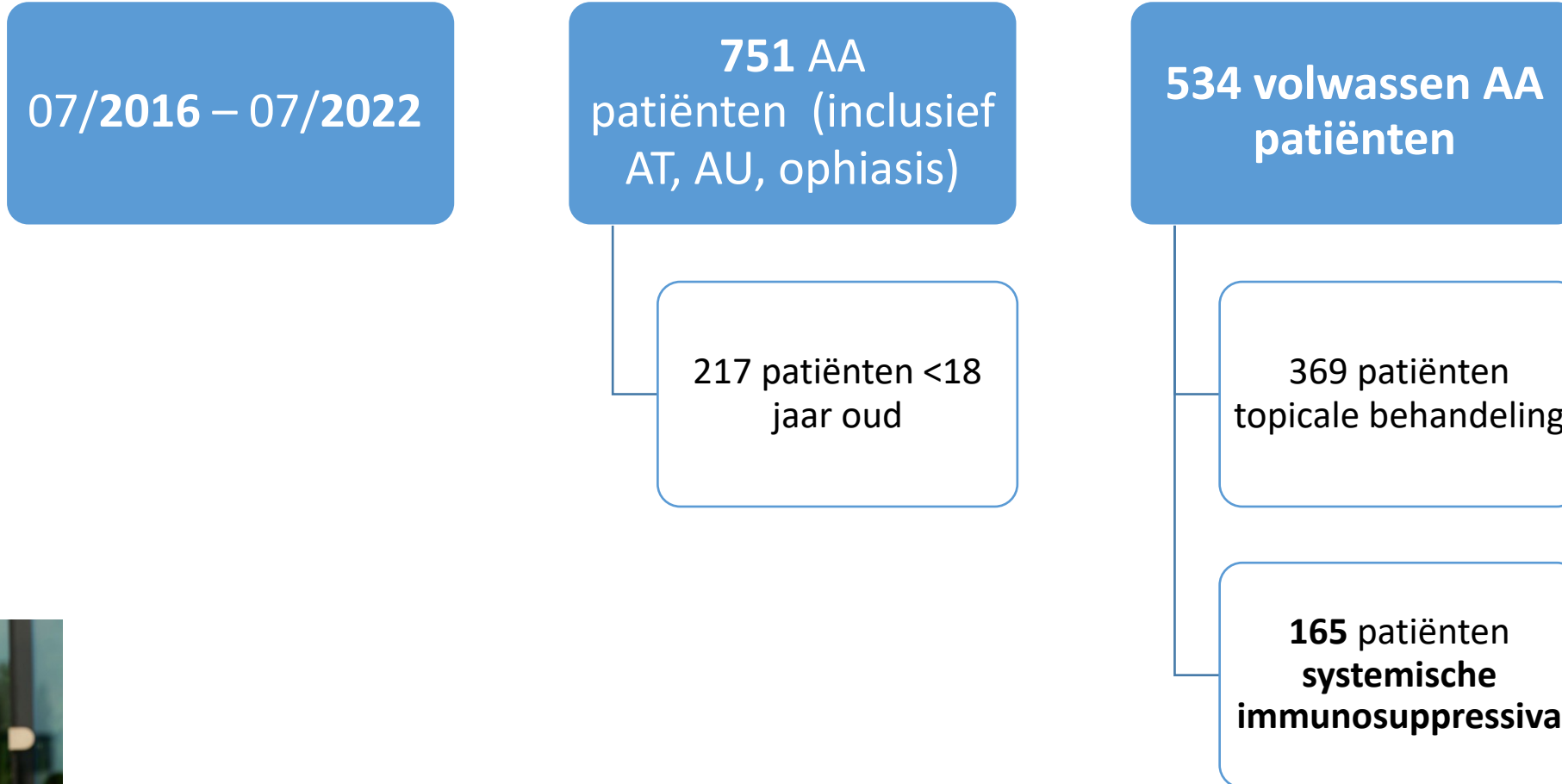
# (Klassieke) systemische behandelingen

- methotrexaat (MTX)
- ciclosporine
- (fumaarzuur, prednison/kenacort i.m.)
- (tofacitinib)

NB deze middelen worden gebruikt voor veel huidziekten (o.a. eczeem en psoriasis)

**De effectiviteit van deze middelen bij AA?**

# Behandeling AA Erasmus MC



Laurents Boom; masteronderzoek GNK

## Patchy Alopecia Areata

One or multiple patches of hair loss  
(conjoined or separate)



## Alopecia Totalis

Total or near-total loss of hair  
on the scalp



## Alopecia Universalis

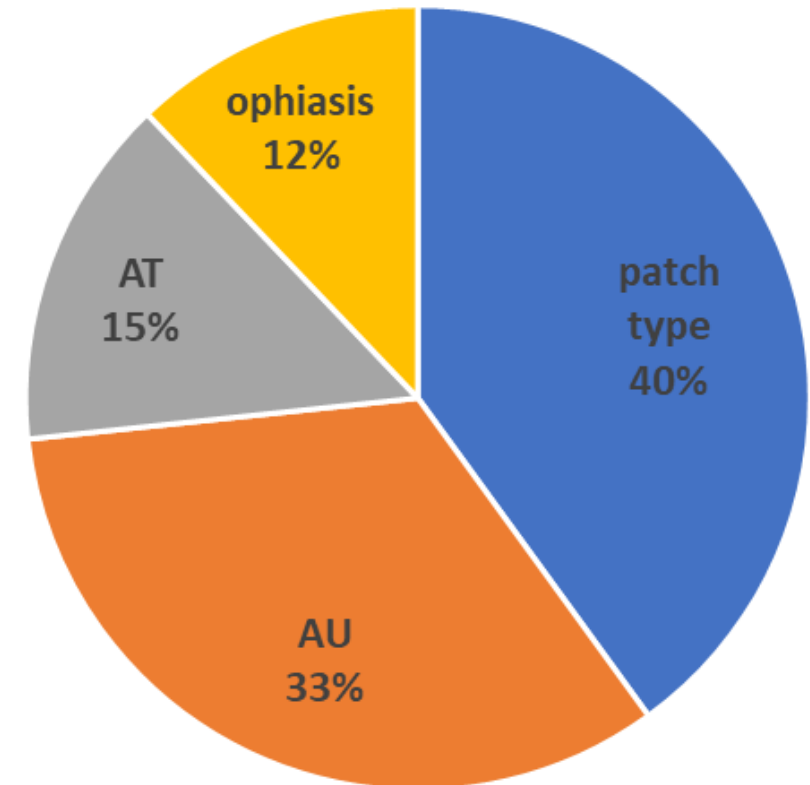
Total or near-total loss of hair  
on the entire body





# Alopecia areata varianten

- **165** volwassen AA patiënten behandeld met **systemische immunosuppressiva**
  - **66** patch-type AA
  - **20** AA ophiasis-type
  - **24** alopecia totalis (AT)
  - **55** alopecia universalis (AU)



# Wimpers / wenkbrauwen

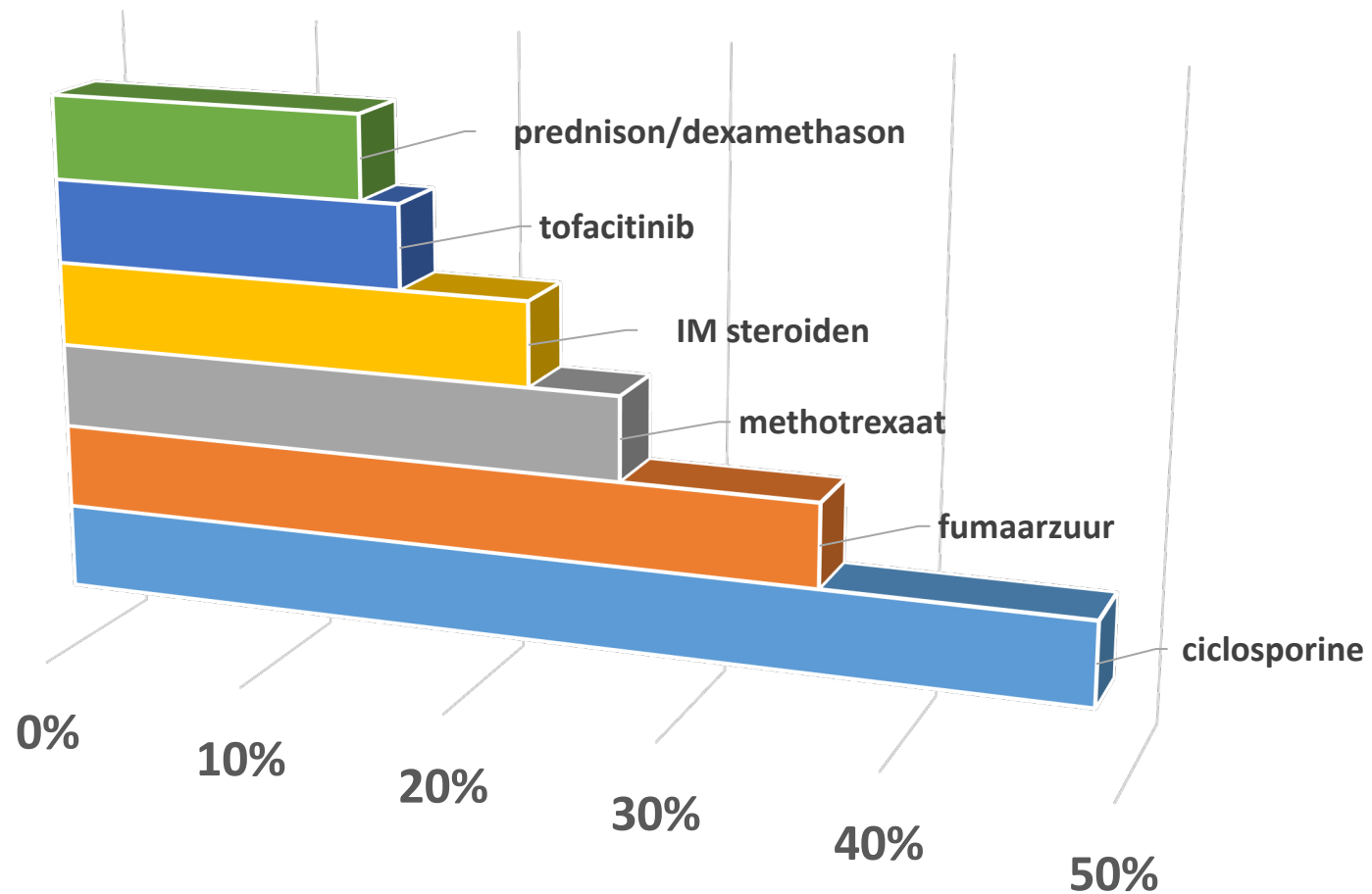
	AA (n=66)	AU (n=55)	AT (n=24)	Ophiasis (n=20)	Total (n=165)
Facial hair involvement, n [%]					
Eyelashes	18 [27.3%]	52 [94.5%]	14 [58.3%]	4 [20.0%]	88 [53.3%]
Eyebrows	27 [40.9%]	53 [96.4%]	19 [79.2%]	3 [15.0%]	102 [61.8%]
Beard	19 [28.8%]	29 [52.7%]	6 [25.0%]	1 [5.0%]	55 [33.3%]
Nail changes, n [%]	6 [9.1%]	10 [18.2%]	5 [20.8%]	0 [0%]	21 [12.7%]
Histopathology, n [%]					
No biopsies	56 [84.8%]	52 [94.5%]	23 [95.8%]	17 [85.0%]	148 [89.7%]
No HP confirmation	5 [7.6%]	0 [0%]	0 [0%]	0 [0%]	5 [3.0%]
HP confirmation	5 [7.6%]	3 [5.5%]	1 [4.2%]	3 [15.0%]	12 [7.3%]

Louis Theroux opens up about his battle with alopecia – what is it and how can it be treated?

LIFESTYLE



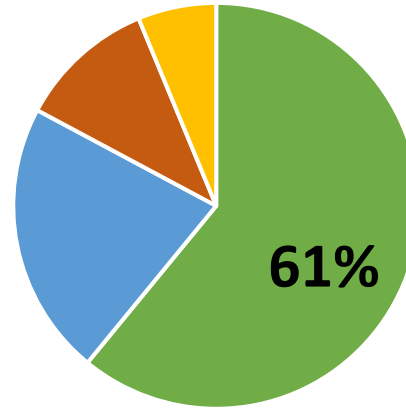
# Behandelingen (n=165)



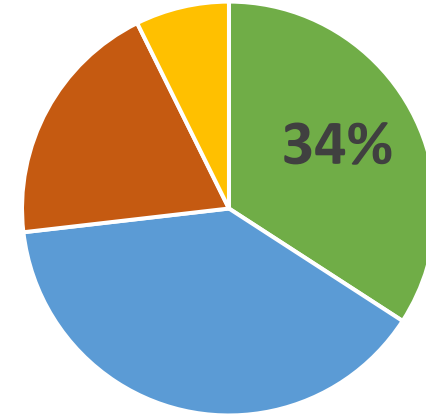
# Therapie respons



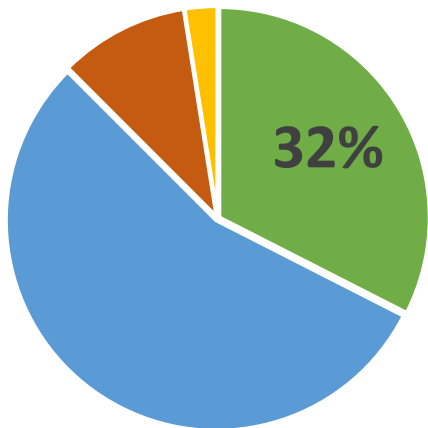
CsA (n=64)



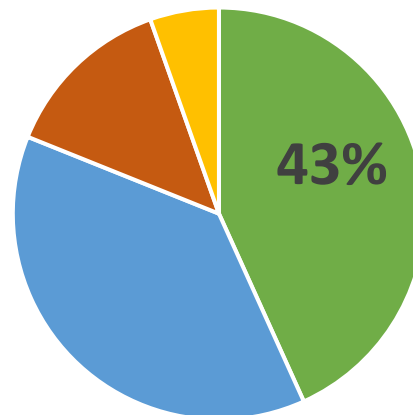
MTX (n=41)



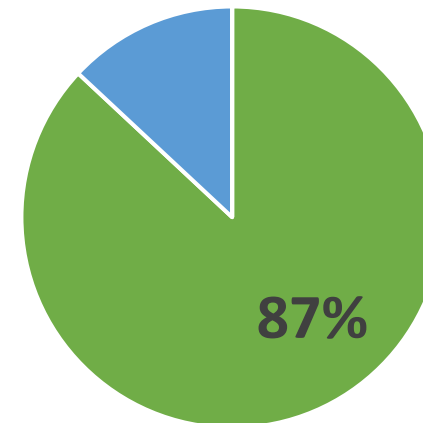
Fumarates (n=40)



(IM) Steroids (n=37)

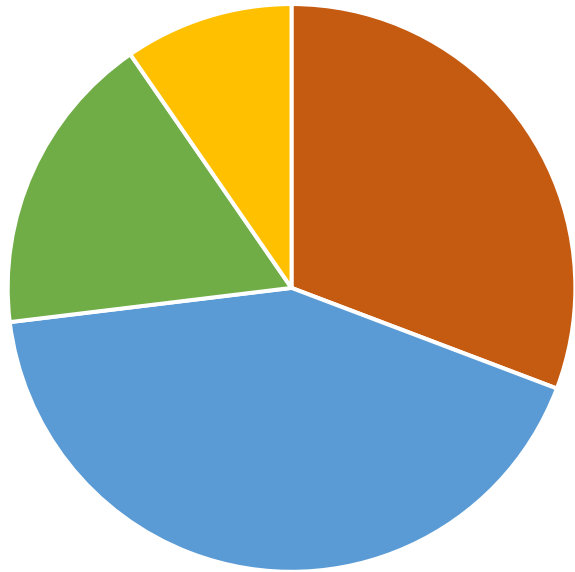


JAKi (n=23)

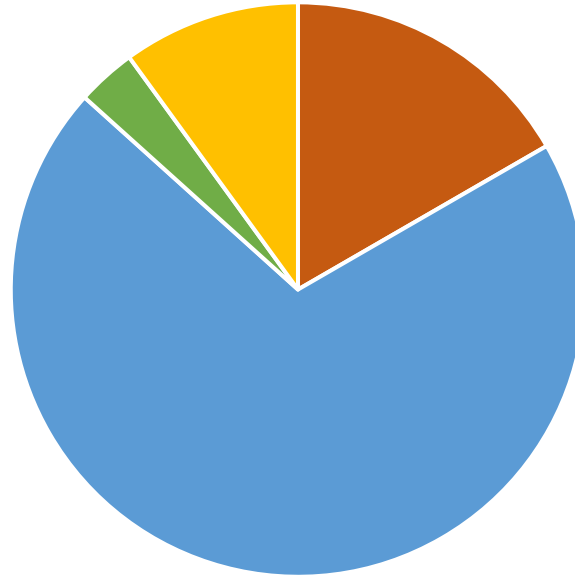


# Redenen voor stoppen

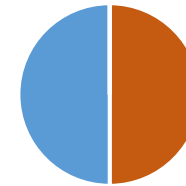
**CsA** (n=64 | 52 discontinued)



**MTX** (n=41 | 30 discontinued)



**JAKi** (n=23 | 2 discontinued)



- side effects
- ineffective
- good response
- other

Belangrijkste reden: onvoldoende effect  
CsA en fumaarzuur relatief veel bijwerkingen

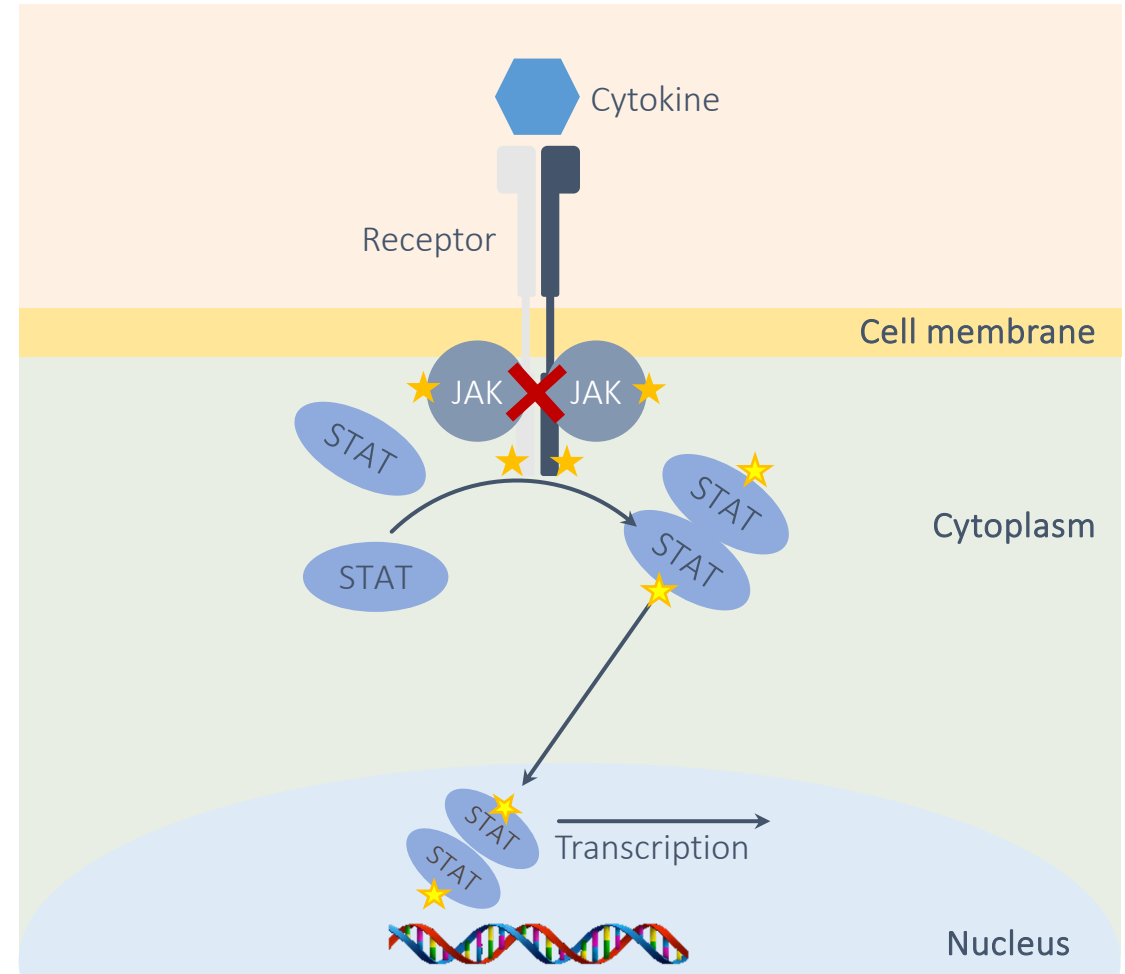
NB meeste patiënten gebruiken hun JAK remmer nog

# Conclusies (1)

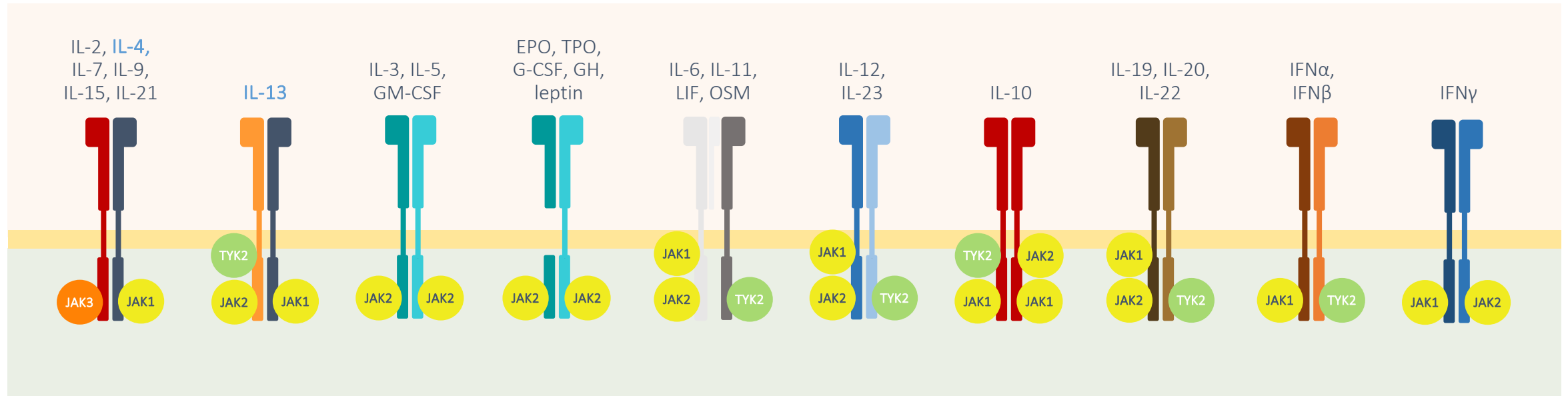
- **Ciclosporine** *lijkt* effectiever dan **MTX**
- Ciclosporine vaker **bijwerkingen** dan MTX
- Fumaarzuur geen rol meer in behandeling AA (ineff. + bijw.)
- JAK remmers zeer veelbelovend (NB tofa, upa/abro vs bari/ritle)

# JAK remmers

- “small molecules”: werken in de cel
- Toedieningsvorm: pil
- Verschillende JAK remmers (bijv. tofacitinig, baricitinib en ritlecinitib)



# Verschilende JAK eiwitten





# JAK remmers zijn niet nieuw!

- Behandeling reuma: **tofacitinib** (2012), **baricitinib** (2017)
- Behandeling eczeem:
  - **baricitinib** (2020), **upadacitinib** (2021) en **abrocitinib** (2022)
  - NB upa ook geregistreerd voor: colitis ulcerosa en ziekte van Crohn

# Eczeem + AA & JAK remmer

**11/2022**

**9/2023**

# Eczeem + AA & JAK remmer

**8/2021**

**10/2022**

# Wanneer komt iemand in aanmerking?

## Criteria voor starten JAK remmer bij AA

- >SALT50
- Na 3-6 mnd behandeling met CsA of MTX
- Max. 10 jaar AA

# Mogelijke bijwerkingen van JAK remmers

- Infecties (koortslip, verkouden/infecties)
- JAKne = soort acne tijdens gebruik JAK remmer
  
- 'labafwijkingen'

# Wanneer geen JAK remmers?

- Actieve kinderwens
- Roken
- Kanker
- Longembolie / trombosebeen / hartproblemen



# Ontwikkelingen AA

- Twee EMA geregistreerde JAK remmers voor AA:
  - **baricitinib** (JAK 1-2 remmer)
  - **ritlecitinib** (JAK3/TYC remmer)
- Vergoeding **baricitinib**: juli 2024????
  - Vragen over impact op QoL van AA en effect behandeling....
- **Ritlecitinib** volgt hopelijk eind 2024

# Controles bij gebruik JAK remmers

- Bloed bij start, 4w, 12w, iedere 3-6 maanden

	start	wk 4	wk 12	3-6 M
<b>Screening</b>				
tuberculose <sup>a</sup>	+			
zwangerschap	+			
HBV/HCV/HIV <sup>b</sup>	+			
<b>Laboratorium onderzoek</b>				
Hb, leukocyten, leuko diff, trombocyten	+	+	+	+
ALAT, GGT	+	+	+	+
serum creatinine	+	+	+	+
cholesterol, triglyceriden	+		+	jaarlijks



# Openstaande vragen

- Welke JAK remmer heeft de beste **effectiviteit**?
- Welk middel heeft het minste **bijwerkingen**?
- **Hoe lang** moet je behandelen?
- Kun je **stoppen** / moet je **afbouwen**?
- Wat gebeurt er bij partiële respons en stoppen? (bijv. bij AT)



# Openstaande vragen

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***a STA<sup>2</sup>R is born!***

- <http://www.sta2r.nl>
- Systemic Treatments Alopecia Areata Registry
- Effectiviteit, veiligheid, effect op kwaliteit van leven

# The AA-Team



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Kelly Kwa  
AIOS dermatologie



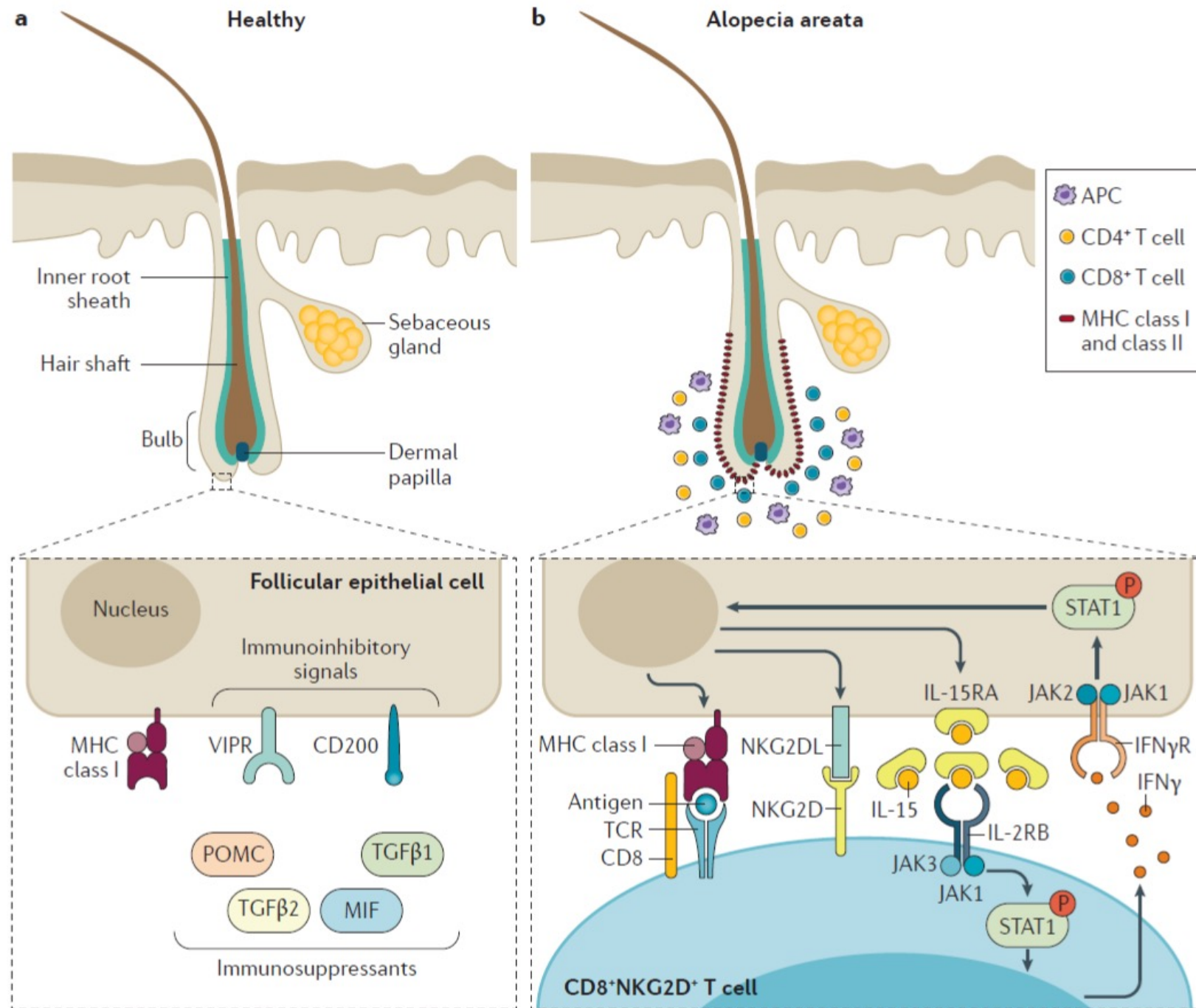
Sophie van Helmond  
Arts-onderzoeker





Dank voor uw AAndacht!





this makes it difficult to assess the magnitude of any benefit. Although a small case series suggests a response to cyclosporine (a calcineurin inhibitor), the benefits are probably too small and inconsistent to justify its use in view of the possible adverse effects<sup>165</sup>. Topical tacrolimus (an immunosuppressant) is ineffective<sup>166</sup>. With the exception of isolated case reports, anti-tumour necrosis

# Global Registry of Alopecia Areata disease Severity and treatment Safety (GRASS)

- A Global eDelphi Exercise to Identify Core Domains and Domain Items
- 92 core data items, 20 noncore data items



Table. Domains and Domain Items for a Global Alopecia Areata Patient Registry\*

Domain	Domain items	Core	Comments
New enrollment/baseline visit			
1. Demographics	Date of birth	Core	None
	Date of enrolment into registry	Core	None
	Gender	Core	None
	Ethnicity	Core <sup>b</sup>	Requires identification of appropriate classification system
	Educational status	Noncore <sup>b</sup>	Requires identification of appropriate classification system
	Current occupation or education	Noncore <sup>b</sup>	Requires identification of appropriate classification system
2. Etiopathogenesis	Location and name of treatment center	Core	None
	History of autoimmune disease	Core	None
	History of allergic comorbidities	Core	None
	Patient comorbidities	Core	None
	Family history of alopecia areata, atopy, or autoimmune disease	Core	Record specific diseases
	Gluten-sensitivity but not diagnosed celiac disease	Noncore <sup>b</sup>	Requires availability of diagnostic biomarkers and criteria
3. Disease triggers	Stressful life event preceding current episode	Core	None
	Environmental history (infection/vaccination history)	Core	None
	Other potential triggers	Core <sup>b</sup>	Requires standardization of expandable list of triggers
4. Baseline history	Days lost from usual activities	Core <sup>b</sup>	Requires further work to define usual activities to facilitate objective measurement
	Adherence to therapy	Core <sup>b</sup>	Requires identification of appropriate scale
5. Baseline clinical features	Fitzpatrick skin phototype	Core	None
	Hair color	Core <sup>b</sup>	Requires development of appropriate classification system
	Nail changes	Core	Including nail pitting, longitudinal ridging, and trachyonychia
	Shedding scale and score	Core	None
	SALT <sup>22,23</sup>	Core	None
	SSA <sup>22</sup>	Core	None
	ALODEX <sup>24</sup>	Core	None
	Trichoscopic signs of activity	Core	Including yellow dots, black dots, exclamation mark hairs, broken hairs, other
	Hair pull	Core	None
	Alopecia areata phenotype	Core	Patch, ophiasis, sisaipho, alopecia totalis, alopecia universalis, diffuse
	Body hair involvement	Core	None
	Eyebrow	Core	None
Eyelash	Core	None	
Beard	Core	None	
6. Investigations	Routine blood tests	Noncore	Including FBC, U&E, and LFTs
	Additional blood tests for autoimmune disease	Core	None
	Scalp biopsy	Noncore	Including anatomical site, number of biopsies, biopsy type, sections, and report
7. Consent	Consent to biomaterial	Core	None
	Consent to images	Core	None
8. Concomitant medication	Concomitant medication	Core	Other than specific alopecia areata medication
9. Current alopecia areata treatment	Topical therapy	Core	None
	Intralesional therapy	Core	None
	Phototherapy	Core	None
	Systemic therapy	Core	None
10. Past alopecia areata treatment	Topical therapy	Core	None
	Intralesional therapy	Core	None
	Phototherapy	Core	None
	Systemic therapy	Core	None
11. Adverse effects	Current treatment	Core	None
	Previous treatment	Core	None
12. Treatment response	Treatment response	Core	Marked improvement, some improvement, no change, some deterioration, marked deterioration

Table. Domains and Domain Items for a Global Alopecia Areata Patient Registry\* (continued)

Domain	Domain items	Core	Comments
13. Management intended at first review	Topical therapy	Core	None
	Intralesional therapy	Core	None
	Phototherapy	Core	None
	Systemic therapy	Core	None
	Current treatment discontinued	Core	None
	Reason for discontinuation	Core	None
14. Prognostic indicators	No. of relapses in 12 mo	Core	None
	Age of onset of alopecia areata	Core	None
	Duration of longest disease episode	Core	<6, 6-12, and >12 mo (if possible to specify)
	Phenotype of longest disease episode	Core	Current disease duration and phenotype will be captured by current history
	Predominant alopecia areata phenotype	Core	Patch, ophiasis, sisaipho, alopecia totalis, alopecia universalis, diffuse
	Previous history of alopecia totalis/alopecia universalis	Core	None
15. PROMs/quality of life measures	Patient-reported symptoms	Core	None
	Patient global assessment	Core	Marked improvement, some improvement, no change, some deterioration, marked deterioration
	AA-QLI/AAQ <sup>25</sup>	Core	None
	AASIS <sup>26,27</sup>	Core	None
	Hairdex <sup>28</sup>	Noncore	None
	DLQI <sup>29,30</sup> /DQOLS <sup>31</sup>	Core	None
	Skindex-29 <sup>32,33</sup>	Noncore	None
	SF-36 <sup>34</sup>	Noncore	None
	Effect on family members, if applicable	Core <sup>b</sup>	Requires further work to define appropriate means of measuring personal and socioeconomic impact
	Bodily symptoms not classified with an official diagnosis	Noncore <sup>b</sup>	Requires appropriate classification system
	Alexithymia assessment questionnaire	Noncore <sup>b</sup>	Requires appropriate classification system
	Questionnaire specifically assessing ability to cope with or process stressors/stress	Noncore <sup>b</sup>	Requires appropriate classification system
16. Alopecia areata organization membership	Membership of alopecia areata associations	Core	Capturing specific group membership
<b>Already enrolled/follow-up visit</b>			
17. Follow-up history	Days lost from usual activities	Core <sup>b</sup>	Requires further work to define usual activities to facilitate objective measurement
	Adherence to therapy	Core	None
18. Follow-up examination general	Nail changes	Core	Including nail pitting, longitudinal ridging, and trachyonychia
19. Follow up examination hair	Shedding scale and score	Core	None
	SALT <sup>22,23</sup>	Core	None
	SSA <sup>22</sup>	Core	None
	ALODEX <sup>24</sup>	Core	None
	Trichoscopic signs of activity	Core	Including yellow dots, black dots, exclamation mark hairs, broken hairs, other
	Hair pull	Core	None
	Hair pigmentation anomaly either during hair loss or hair regrowth	Core	Spontaneous or treatment associated
	Alopecia areata phenotype	Core	Patch, ophiasis, sisaipho, alopecia totalis, alopecia universalis, diffuse
20. Follow-up treatment response	Body hair involvement	Core	None
	Eyebrow	Core	None
	Eyelash	Core	None
	Beard	Core	None
	Response	Core	Marked improvement, some improvement, no change, some deterioration, marked deterioration
21. Follow-up adverse effects	Hair regrowth of ≥50%	Core	Requires further work to identify meaningful response for patients
	Serious adverse events attributed to current treatment	Core	None
22. Follow-up investigations	Routine blood tests	Noncore	FBC, U&E, and LFTs
	Other investigations	Noncore	Other blood investigations or biopsies

## Spreekuur

# Haar advies spreekuur

Op het haar advies spreekuur worden patiënten gezien met haaruitval en problemen van de haren en hoofdhuid.

## Uw bezoek

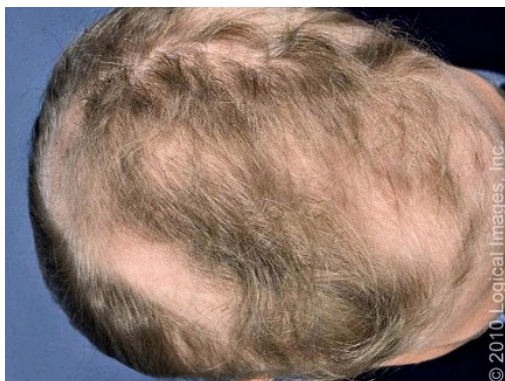
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### Wat gaan we doen?

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Op dit spreekuur zal gekeken worden naar het haarprobleem met als doel om uw vragen en die van uw verwijzend specialist over de diagnose en/of de behandeling van het haarprobleem te beantwoorden. Er vindt een uitgebreid gesprek plaats (anamnese) en een lichamelijk onderzoek van de haren en de hoofdhuid. Vaak wordt ook trichoscopie verricht, een onderzoek met een digitaal vergrootglas met ingebouwd (gepolariseerd) licht, om de hoofdhuid en de basis van de haren goed in beeld te krijgen. Er zal uitleg gegeven worden over onze bevindingen en adviezen. Deze adviezen schrijven wij ook in een brief aan de verwijzend specialist. Deze zal met u een eventuele behandeling opstarten. Op het haar advies spreekuur zal geen behandeling gestart worden. Uw bezoek aan het haar advies spreekuur zal een éénmalig bezoek zijn, waarna u terugverwezen wordt naar uw verwijzend specialist.





# Respons op therapie (patch type)

**Table 6.1.** Alopecia areata systemic treatment response

Response, n[%]	Cyclosporine	Fumarates	Methotrexate	IM Steroids	JAK inhibitors	Prednisone
No response	2 [9.5%]	3 [27.3%]	1 [7.7%]	3 [21.4%]	-	-
Impairment	2 [9.5%]	2 [18.2%]	2 [15.4%]	1 [7.1%]	-	-
<b>Improvement</b>	<b>15 [71.4%]</b>	6 [54.5%]	7 [53.8%]	9 [64.3%]	<b>6 [100.0%]</b>	1 [100.0%]
Unknown	2 [9.5%]	-	3 [23.1%]	1 [7.1%]	-	-

Pearson Chi-square test = .695

# Kennislacunes

- Het is onbekend of behandeling acute alopecia (snelle progressie) de kans verkleint op chronische AA