

What constitutes clinical benefit for trials of cNF?

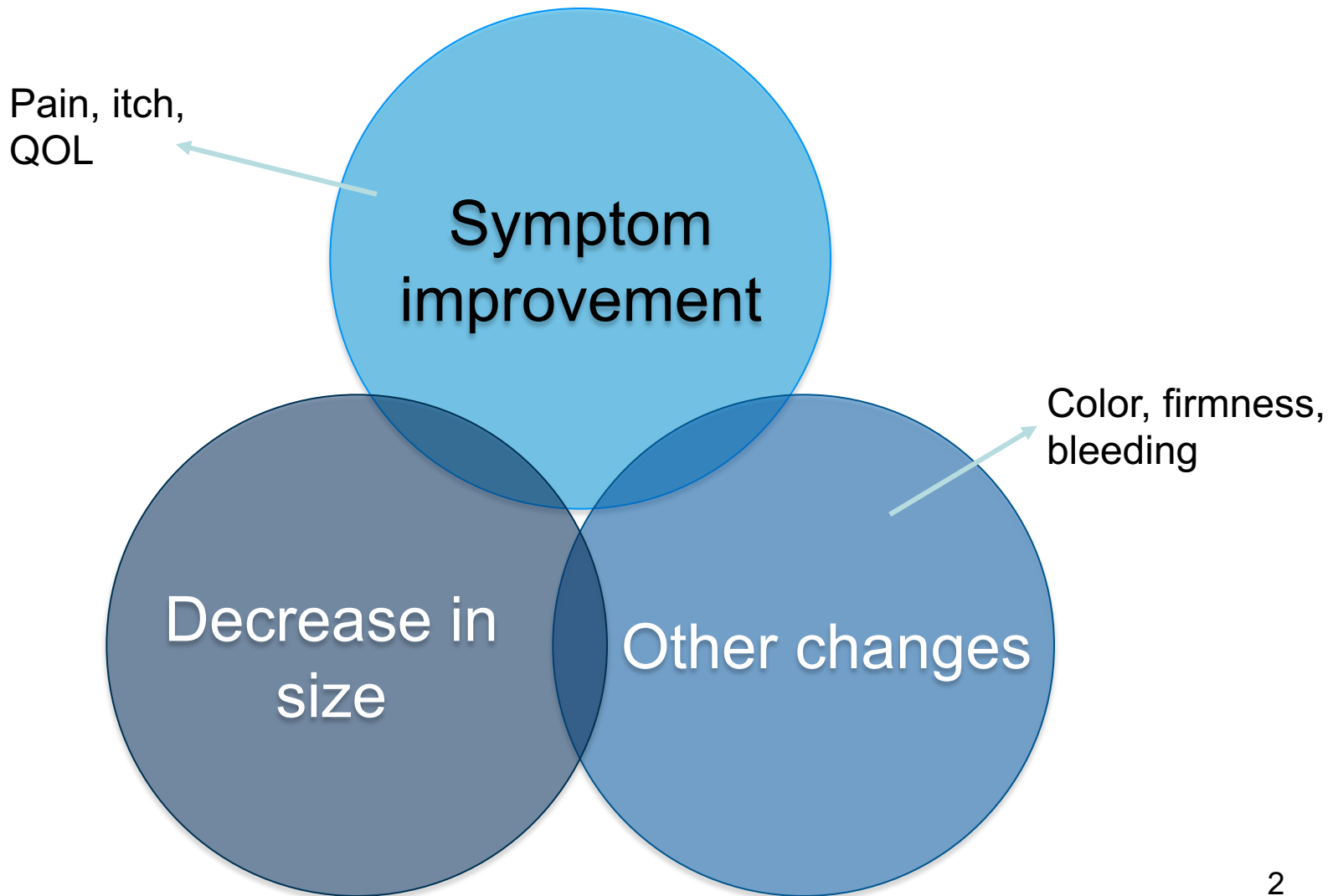
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Dermatology Branch, NIH

REiNS Winter Meeting 2018
Bethesda, MD



Response Evaluation In Neurofibromatosis Schwannomatosis
INTERNATIONAL COLLABORATION

What are the domains of clinical benefit?



What are the domains of clinical benefit?

Other changes



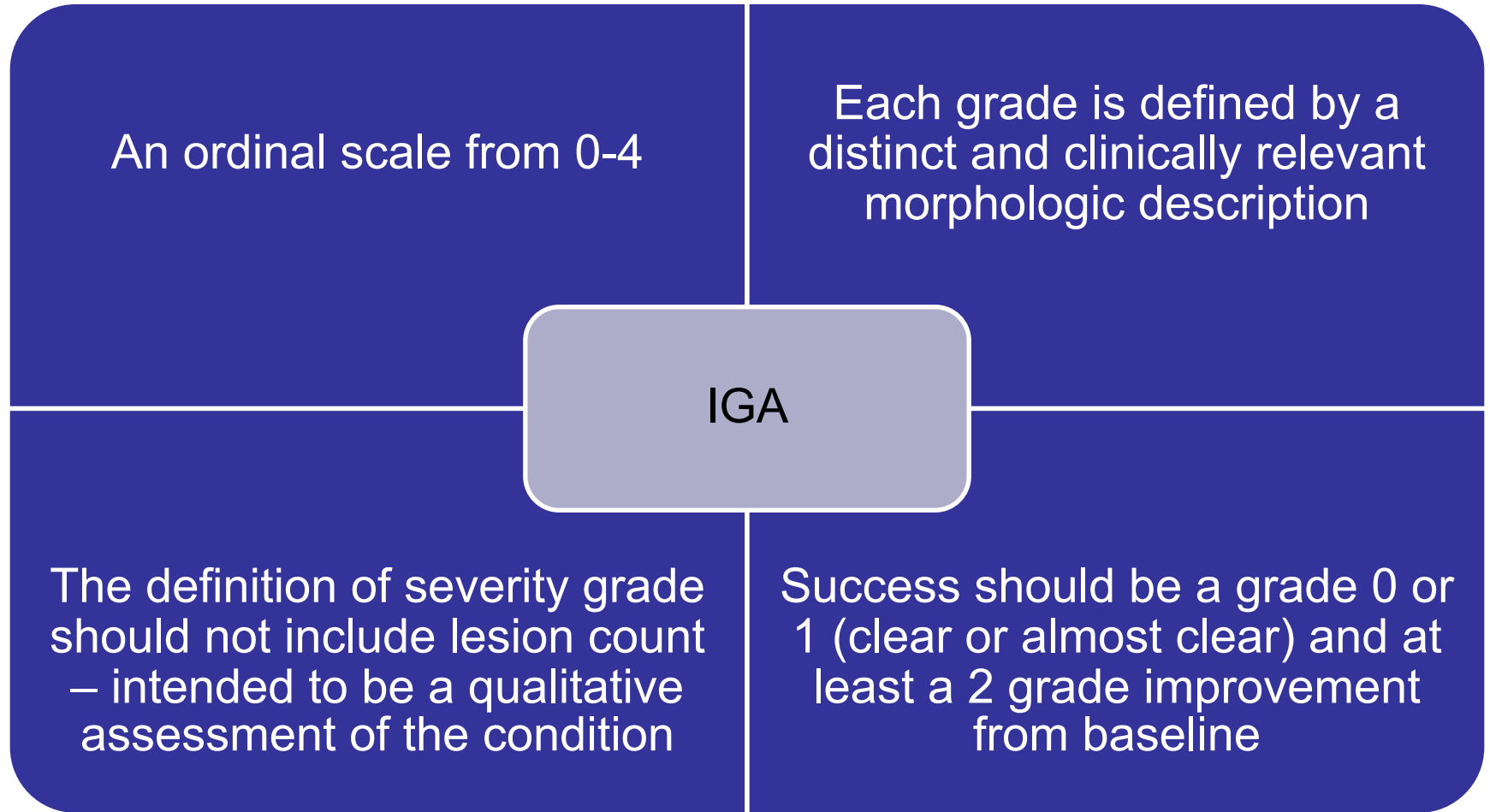
To date, there are no validated clinical outcome assessments to measure clinical treatment effects on cutaneous neurofibromas

Objective measures of size or volume change have been proposed, but are not validated in this population

The FDA recommends **GLOBAL ASSESSMENTS** from the patient and from the investigator for clinical trial



What is an Investigator Global Assessment (IGA)?



Example of IGAs: psoriasis

Score	Short description	IGAs
0	Clear	Inflammatory present
1	Almost clear	Pink coloration;
2	Mild	Thinning; pink to white; predominantly fine
3	Moderate	Moderate thickening; clearly defined; moderate thickening;
4	Severe	Well defined edges; bright red; severe/coarse thickening for all lesions




Example of IGAAs: eczema



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Example of IGAs: lateral canthus rhytides

Score	Wrinkle s rest		
0	Absent		
1	Minimal		thin 1.5cm radius of and may be minimally
2	Mild		extending between 1.5- lateral canthus and
3	Moderate		wrinkles, extending radius of the lateral tightly etched
4	Severe		extending 2.5cm radius and may be deeply

Example of IGAs: epidermal cGVHD

Score	Short
0	Clear
1	Almos
2	Mild
3	Moder
4	Sever



Score	Short
0	Clear
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2	Mild
3	Moder
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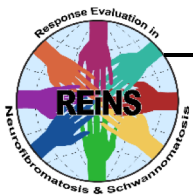
Other future considerations

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Other future considerations

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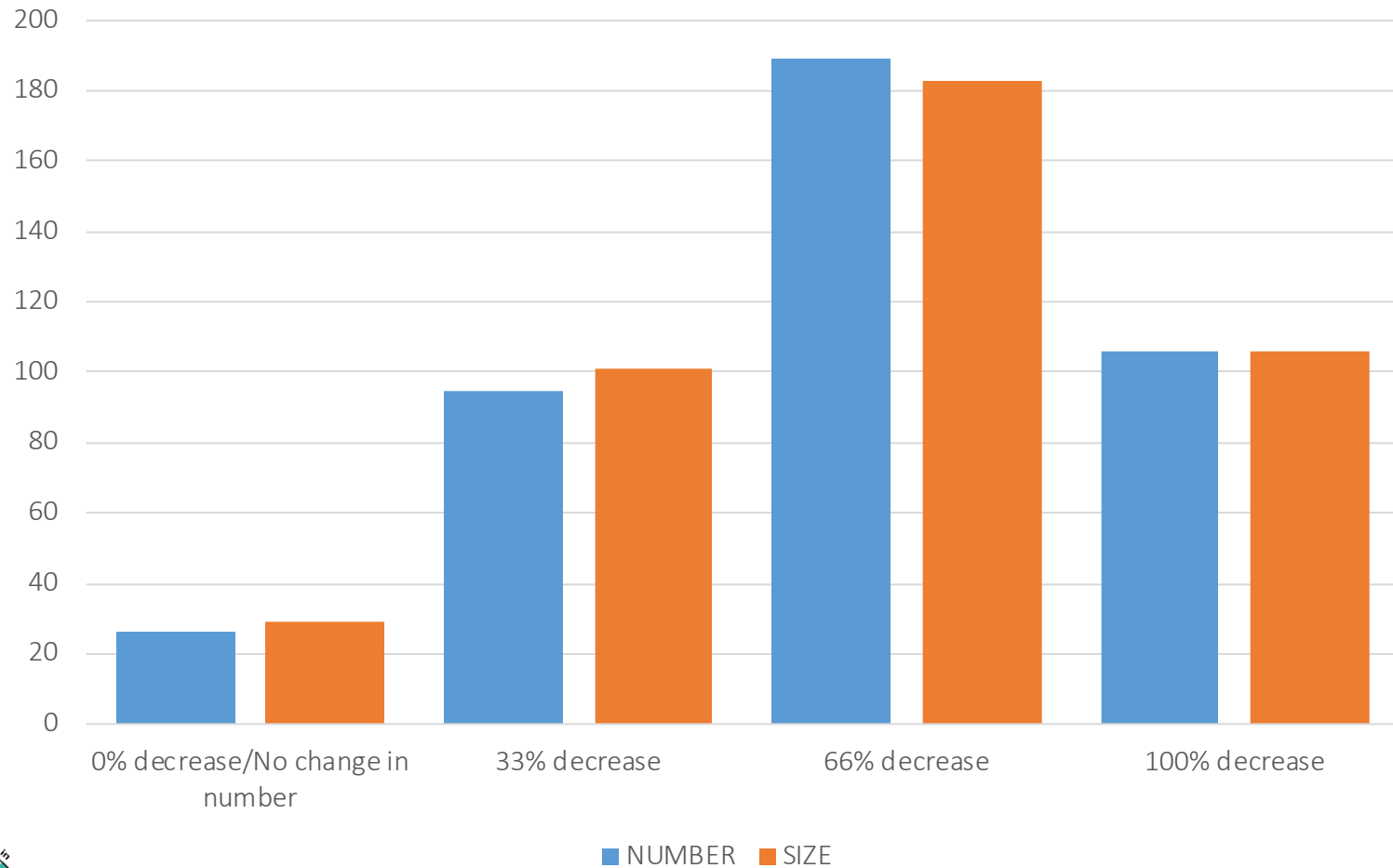
independent

24 compared

“The patient-focused drug development meetings conducted to date have given FDA a deeper appreciation for the expertise that patients and caregivers can bring to the process and the value of incorporating their voice.”



When thinking about the raised cutaneous neurofibromas that bother you the most, what is the minimum decrease that would be acceptable to you after participating in a treatment trial?



Comment: patients do not demand 100% shrinkage in clinical trials

How do you agree with the following statements?

I would prefer a scar instead of a cNF



I would prefer skin color change instead of a cNF



I would be satisfied if my raised cNFs were flat



I would accept resolution of pain with no visible change of cNFs



I would accept resolution of itch with no visible change of cNFs



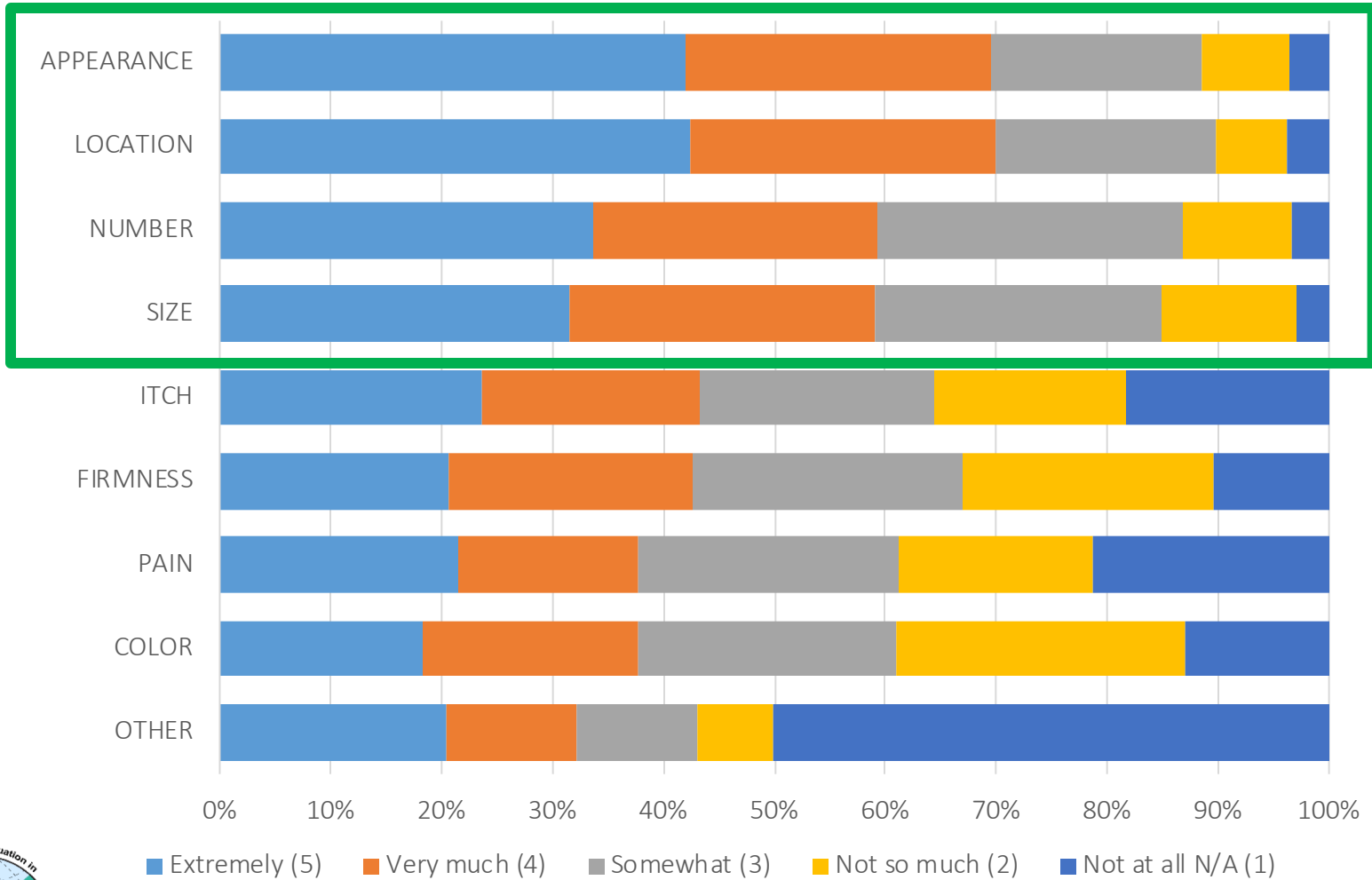
0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

■ Strongly Agree ■ Agree ■ Neither Agree nor Disagree ■ Disagree ■ Strongly Disagree



Comment: scars and pigmentary changes are better than tumors

How much does each FEATURE of your **raised** cutaneous neurofibromas bother you (physically, cosmetically, or emotionally)?



Comment: appearance (size, number) is key driver for patients

Patient view on clinical benefit

Important

Number

Size

Elevation

Appearance

Location

Less important

Itch

Pain

Firmness

Residual scar

Color change

cNF IGA draft version 1

Score	Short descriptor	Detailed descriptor for region of interest (ROI)
0	Clear	No residual tumor; Scar or pigmentary change may be present
1	Almost clear	Flat tumors, may have discoloration
2	Mild	Low number and/or size of raised tumors that cause mild disfigurement of the underlying skin
3	Moderate	Moderate number and/or size of raised tumors that cause moderate disfigurement of underlying skin
4	Severe	High number and/or size of raised tumors that cause severe disfigurement of underlying skin



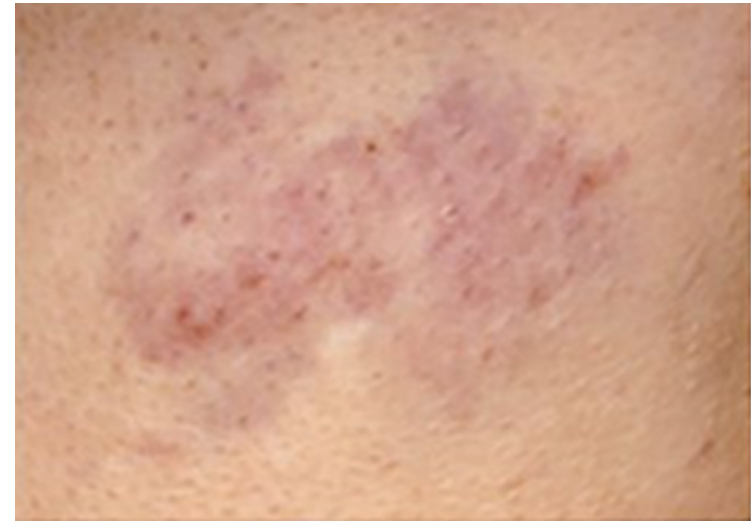
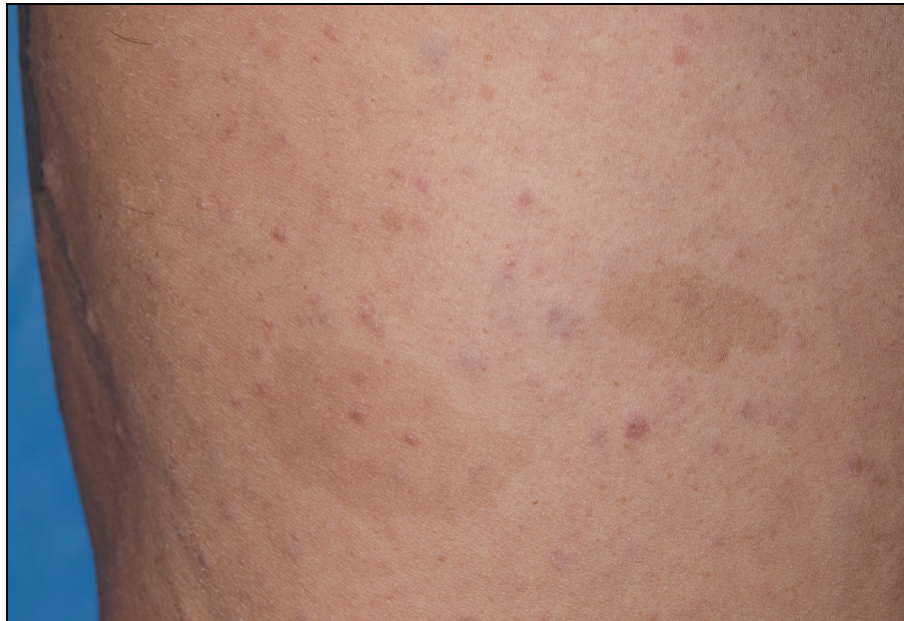
cNF IGA_draft_v1

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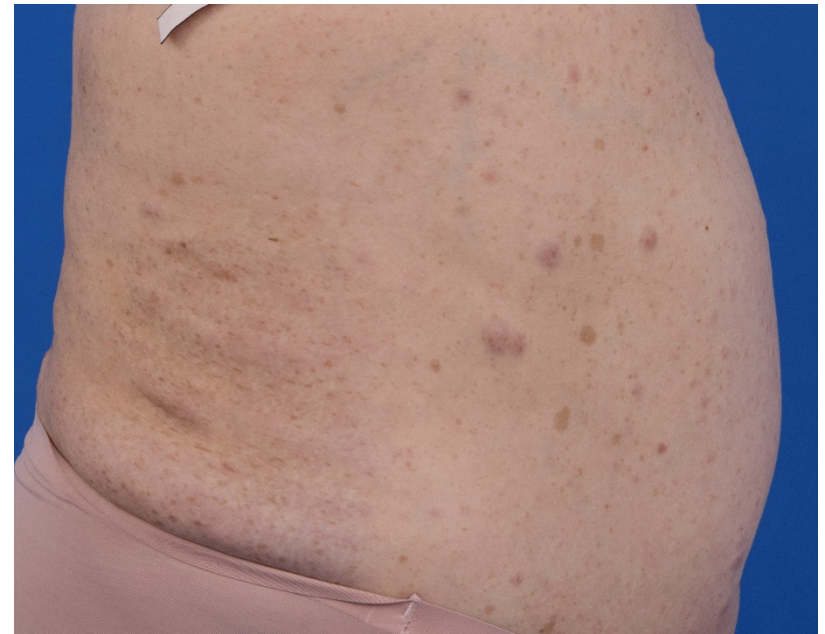
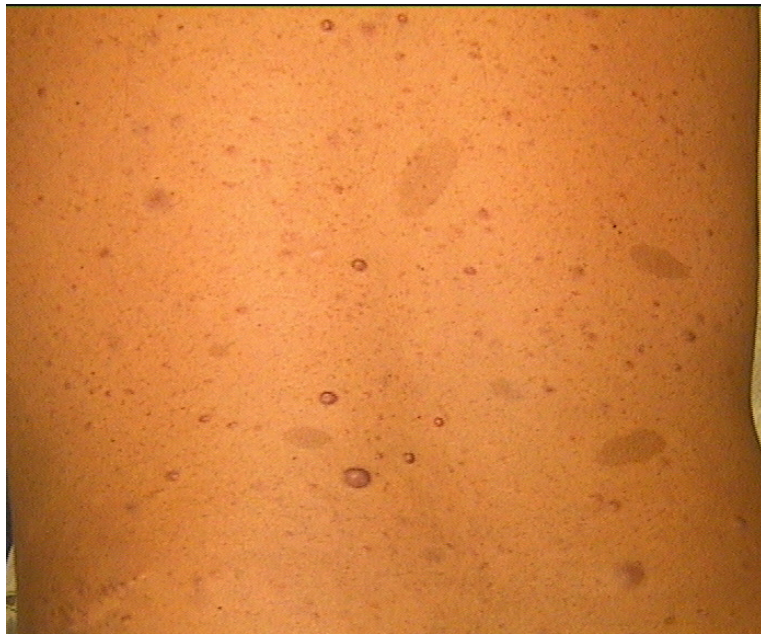
cNF IGA_draft_v1

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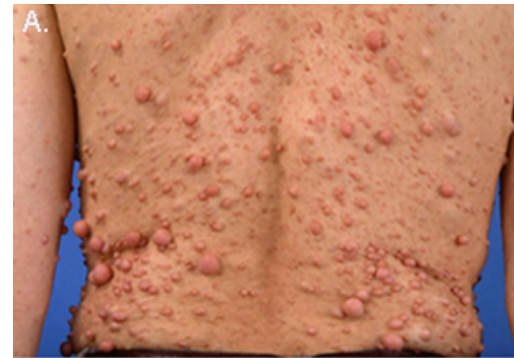
cNF IGA_draft_v1

Score	Short descriptor	Detailed descriptor for region of interest (ROI)
2	Mild	Low number and/or size of raised tumors that cause mild disfigurement of the underlying skin



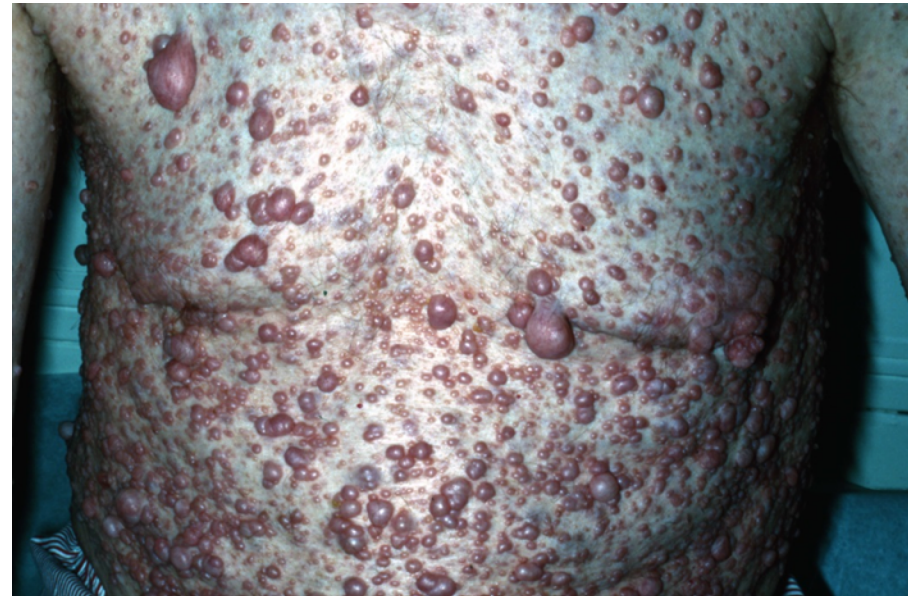
cNF IGA_draft_v1

Score	Short descriptor	Detailed descriptor for region of interest (ROI)
3	Moderate	Moderate number and/or size of raised tumors that cause moderate disfigurement of underlying skin



cNF IGA_draft_v1

Score	Short descriptor	Detailed descriptor for region of interest (ROI)
4	Severe	High number and/or size of raised tumors that cause severe disfigurement of underlying skin



cNF IGA draft version 1

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Patient view on clinical benefit

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Color change

Acknowledgements

- The Cutaneous Neurofibroma Working Group of REiNS
- The patients, caregivers, and patient advocates who take part in our program and the research we perform
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