STAR-JIA

STEROID TREATMENT TRIAL IN JUVENILE IDIOPATHIC ARTHRITIS

pGTI Training

Presentation - 2024

Background

Steritas paediatric Glucocorticoid Toxicity Index pGTI

- provides a systematic approach to assessing steroid-toxicity in children between the ages of 2 and 18 years.
- provides weighted scores of steroid-toxicity.
- fast, accurate, and easy to implement.

Glucocorticoids can severely impact growth and development in children, lead to adverse events in puberty, and can affect overall wellness throughout adulthood. To fully address these impairments, the pGTI:

- Includes growth as an entirely new domain.
- Considers age-related references such as height, and gender-specific reference ranges for blood pressure and other parameters.
- Assesses neurological side effects unique to the paediatric population.
- Adjusts domain weights to score those steroid-toxicities that are specific to children.

The first validated clinical outcome assessment of steroid-toxicity in children.

The STOX Suite (GTI, pGTI and GTI-MD) has been licensed in 25+ disease indications, across 1100 sites in 80 countries across the world.

STERITAS

pGTI CRF

This Case Reporting Form (CRF) is used to collect data for calculation of Paediatric Glucocorticoid Toxicity Index (GTI) scores.

- pGTI should be completed at every visit.
- Completed by a Clinician/CNS on the delegation log.
- The pGTI assessment should be completed on the latest version of the pGTI Assessment Form shared with sites as part of the ISF documentation.
- Data on the pGTI Assessment Form should be entered on the CRF in the trial database.
- Completed pGTI assessments should be scanned into the participant's medical records AND filed in the ISF or if stored in a separate folder, a file note should be kept in the ISF to indicate the location of the completed assessments.
- Staff should consider whether data entered on the pGTI eCRF indicates that an AR at week 6 or week 12 visit or an SAE should be reported.

pGTI CRF: STAR- JIA recruit *baseline visit*

- Baseline visit: participant not had systemic corticosteroids so should score 0 or no for all data-fields (in majority of cases)
- **ONLY** recording items on pGTI which the assessor feels are secondary to corticosteroids e.g., if sleep poor secondary to ADHD or already has acne before starts steroids DO NOT score these items on pGTI
- Participants 10 years and over complete Tanner puberty stage (and again at 52 week visit to assess whether any delayed puberty)

pGTI CRF: STAR- JIA recruit

Week 6, 12, 24 and 52 visits

SECTIONS:

- Medications for lipid, BP or glucose control (already capture in concomitant meds review)
- Height, weight, BP completed at clinic visit
- Additional bloods: HbA1C and LDL
- Blood pressure events
- Steroid myopathy
- Skin toxicity
- Neuropsychiatric effects
- Infections
- Damage checklist

Ask about in history

- **ONLY** recording items on pGTI which the assessor feels are secondary to corticosteroids

pGTI CRF

MEDICATIONS INSTRUCTIONS

At Baseline/Visit 1, record whether or not the patient is taking medication(s) for one or more of these conditions. You do not need to record the precise medication names and doses in this worksheet.

At all other visits (i.e., visits except Baseline/Visit 1) when pGTI is assessed, evaluate the overall medication status for each of these three conditions, i.e., glucose control, lipid control, and blood pressure, in comparison to the medication status at the previous pGTI assessment.

The following questions can be used in support of this assessment:
- Has the overall intention been to increase treatment with a medication?
- Has the overall intention been to decrease treatment with a medication?
- Has the overall intention been no change to treatment with a medication?

Examples:
- If the patient previously required only one medication to treat hypertension but is now on two, that represents an increase.
- If the patient previously took a medication for lipid control but now requires none, that represents a decrease.
- If a blood pressure medication has been poorly tolerated and therefore replaced by another, that represents no change.

pGTI CRF

MEDICATIONS (baseline visit)		
Glucose control	Yes	No
Lipid control	Yes	No
Blood Pressure	Yes	No

Please record the medications in the Concomitant Medications form(s)

MEDICATIONS (follow-up visit)			
Glucose control	Increased	No change	Decreased
Lipid control	Increased	No change	Decreased
Blood Pressure	Increased	No change	Decreased

pGTI CRF

HEIGHT and WEIGHT, BLOOD PRESSURE, HbA1c and LDL

(these will be read-only, displaying from the Vital Signs and Clinical Laboratory forms that you must complete at the same visit before entering data into the pGTI)

BLOOD PRESSURE EVENT:

•**Hypertensive emergency:** The blood pressure has reached levels that are damaging organs. Hypertensive emergencies generally occur at blood pressure levels exceeding 180 mmHg systolic OR 120 mmHg diastolic but can occur at lower levels in patients whose blood pressures have not been elevated before. Complications can include: stroke, loss of consciousness, memory loss, myocardial infarction, hypertensive retinopathy or nephropathy, aortic dissection, angina, pulmonary edema.

Hypertensive emergency Present Not Present

•**PRES** (Posterior reversible encephalopathy syndrome: A clinical-radiological entity. Clinical features may include headaches, altered mental status, seizures, and vision loss, depending on the neuroanatomical regions affected. Characteristic magnetic resonance imaging (MRI) findings include vasogenic edema involving the white matter that predominantly affects the posterior occipital and parietal lobes of the brain, but other brain regions may also be affected. Confirmation by MRI is required, as is exclusion of other potential causes (including hypertensive emergency).

Hypertensive emergency Present Not Present

Please ensure any events meeting the criteria for reporting as an Adverse Reaction (week 6/12) and/or Serious Adverse Event (SAE) for STAR-JIA are entered into those forms

pGTI CRF

STEROID MYOPATHY

Glucocorticoid-induced myopathy is defined as symmetrical weakness of the proximal muscles and/or neck flexors associated with glucocorticoid therapy, and NOT due to any other apparent cause. Muscle enzymes are typically within normal limits.

Glucocorticoid-induced Myopathy Definitions

- MINOR (Grade 1): is mild weakness that does NOT functionally limit the patient.
- MODERATE (Grade 2): is mild weakness that DOES functionally limit the patient, interfering with normal daily activities.
- MAJOR (Grade 3): is severe weakness such as difficulty rising from a chair without assistance

Steroid myopathy: choose

None | Minor (Grade 1) | Moderate (Grade 2) | Major (Grade 3)

CHAQ will assess function – if no weakness score 0;
if weakness use CHAQ to help grade

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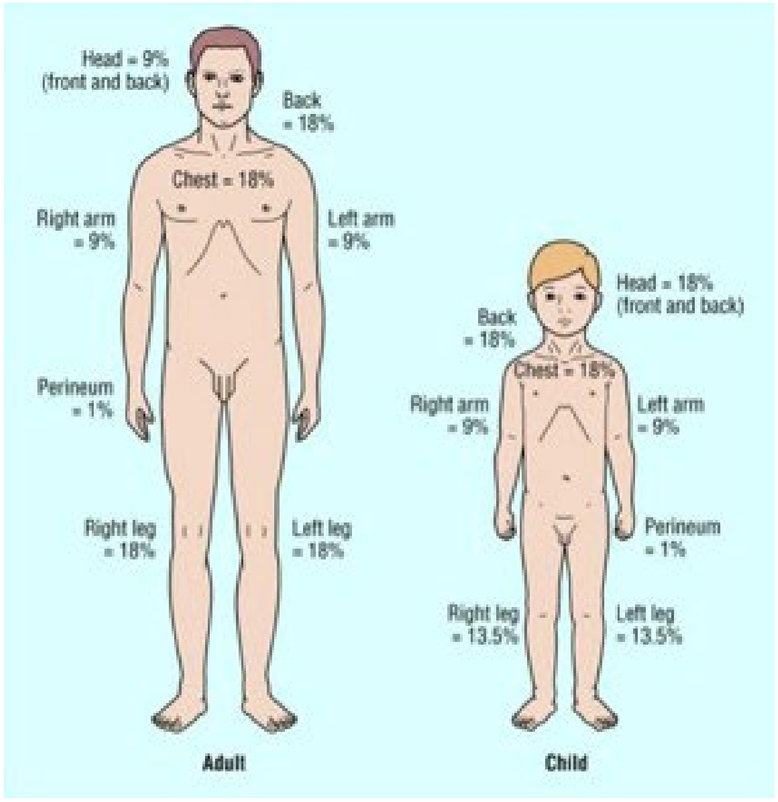
pGTI CRF

SKIN TOXICITY



Acneiform rash

•**Grade 1** - Papules and/or pustules covering < 10% body surface area (BSA), which may or may not be associated with symptoms of pruritus or tenderness

•**Grade 2** - Papules and/or pustules covering 10 - 30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; OR associated with psychosocial impact; OR limiting instrumental activities of daily living (ADL)

•**Grade 3** - Papules and/or pustules covering >30% BSA, which may or may not be associated with symptoms of pruritus or tenderness; OR limiting self care ADL;
OR associated with local superinfection with oral antibiotics indicated

•**Grade 4** - Papules and/or pustules covering any % BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection with IV antibiotics indicated;
OR life- threatening consequences

- **ONLY** recording items on pGTI which the assessor feels are secondary to corticosteroids

pGTI CRF

SKIN TOXICITY

Acneiform rash	None	Grade 1	Grade 2	Grade 3	Grade 4 or higher

Easy bruising

•Grade 1 - Localized (often unifocal) or in a dependent area (unifocal)
•Grade 2 - Generalized (multi-focal); OR associated with psychosocial impact

Easy bruising	None	Grade 1	Grade 2

Hirsutism

•Grade 1 - Hirsutism that the patient is able to camouflage by periodic shaving, bleaching, or removal of hair
•Grade 2 - Hirsutism that requires daily shaving or consistent destructive means of hair removal to camouflage; OR associated with psychosocial impact.

Hirsutism	None	Grade 1	Grade 2	
Striae •Grade 1 - Covering < 10% BSA •Grade 2 - Covering 10 - 30% BSA •Grade 3 - Covering >30% BSA				
Striae	None	Grade 1	Grade 2	Grade 3
Erosions/Tears/Ulcerations	Present	Not Present		

pGTI CRF

NEUROPSYCHIATRIC EFFECTS

Sleep Problems

•**Grade 1:** [Change in sleep latency (< 30min) OR infrequent (1 or 2) night awakenings] AND total sleep < 10 hours (3-5 yrs), < 9 hrs (6+ yrs) AND no daytime impact
•**Grade 2**: [Sleep latency 30-60 min OR occasional (3-4) night awakenings] AND total sleep < 9 hours (3-5 yrs) < 8 hours (6+ yrs) AND mild daytime impact
•**Grade 3:** [Severe sleep disturbance with latency >60min OR frequent (5) night awakenings AND total sleep < 8 hours (3-5yrs) < 7 hrs (6+ yrs) AND severe daytime impact

Sleep Disturbance	Grade 0	Grade 1	Grade 2	Grade 3 or higher

Mood regulation

•Grade 1: Minor irritability, agitation, subjective anxiety, not daily
•Grade 2: Frequent mood swings, aggressive outbursts, depressive episodes, euphoria, overfamiliarity…
•Grade 3: Persistent irritability, depression with loss of activity, suicidal, or elevated mood, irrational ambitions

Mood	Grade 0	Grade 1	Grade 2	Grade 3 or higher

Cognitive Impairment

•Grade 1: Subjective learning difficulties (reduced attention span)…
•Grade 2: Impaired memory, objectively recognised, loss of immediate recall…
•Grade 3: Substantial learning difficulties leading to impaired educational progress

Cognitive Impairment	Grade 0	Grade 1	Grade 2	Grade 3

pGTI CRF

Psychosis/steroid induced violence

o Other neuropsychiatric toxicities, including psychosis and glucocorticoid-induced violence toward self or others at all assessment time points, are also considered in pGTI scoring.

o Psychosis is defined in the pGTI as hallucinations, delusions, or disorganized thought process occurring in the absence of mania, delirium, or depression.

Steroid-induced violence	Present	Not Present
Psychosis	Present	Not Present

pGTI CRF

INFECTIONS

INFECTIONS GRADING

Infection Definitions

•No significant infection = No specific infections or serious infections, grade 3 or greater
•Specific Infections - Oral or vaginal candidiasis or zoster infections without post-herpetic neuralgia or eye involvement
•Grade 3 - Intravenous antibiotic, antifungal, or antiviral intervention or hospitalization indicated OR radiologic or operative intervention indicated OR herpes zoster complicated by post-herpetic neuralgia or eye involvement
•Grade 4 or 5 - Life-threatening consequences; urgent intervention indicated OR death from infection

Infections

Grade 0 (none) Oral/Vaginal Candidiasis (Grade 2) Localized Zoster (Grade 2) Grade 3

Grade 4 Grade 5

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pGTI CRF

Damage Checklist for Baseline & Follow-up Visits

- Does the patient have any of the following at baseline?
- Has the patient had any of the following since the last evaluation?

Endocrine:

Symptomatic adrenal insufficiency

Pubertal Delay/Sex Hormone Axis Interruption

If post-pubertal, maintenance of the same Tanner stage for more than one year Delayed start of puberty
New-onset secondary amenorrhea or oligomenorrhea

Ocular

Central serous retinopathy
New-onset or worsened elevation of intra-ocular pressure requiring treatment or change in treatment Posterior sub-capsular cataract

Gastrointestinal Tract

Gastrointestinal perforation (occurring in absence of regular nonsteroidal antiinflammatory drug use) Peptic ulcer disease confirmed by endoscopy (excluding H. pylori)

Bone Health/ Musculoskeletal

Yes, Osteonecrosis of 1 joint Yes, Osteonecrosis of > 1 joint
Yes, insufficiency fracture of 1 bone Yes, insufficiency fracture > 1 bone Yes, 1 tendon rupture
Yes, > 1 tendon ruptures

Glucose Tolerance

Diabetic retinopathy Diabetic nephropathy Diabetic neuropathy

pGTI CRF: STAR- JIA recruit

Week 6 visit

Ask in history:

- Medications
- Any muscle weakness? If yes any impact on function
- Have you noticed any problems with your skin since having steroids such as new or worse spots, more bruises, stretch marks, more hair on your body?
- Period irregularities (girls)
- Do you think the steroids have affected your sleep, mood, how your brain works?
- Any new medical problems (due to steroids)

Case 1:

- Waking up 2 times a night for first 3 days after drip, grumpy for 3 days
- No skin changes
- No muscle weakness and CHAQ 0
- No new concomitant meds or medical problems

- SCORED FOR SLEEP DISTURBANCE GRADE 1 AND MOOD REGULATION GRADE 1
- **As week 6 visit AR also needs to be recorded for both**

Considerations for completion

Paper

Use paper when discussing with families

Give extra time

To categories such as sleep

Other tips

Only record items if in your opinion they are secondary to corticosteroids

Need to ask about:

- Period irregularities (girls)
- Skin – acne, striae, bruising, increased hair
- Sleep, mood, cognition
- Muscle weakness
- Any new medical problems (due to steroids)

Thank You

For Your Attention