ADVANCES IN Cancer IMMUNOTHERAPY™

Melanoma Immunotherapy

Nursing Perspective on Immune-Related Adverse Events: Patient education, Monitoring & Management

AMERICAN ACADEMY OF EMERGENCY MEDICINE

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UCSF Medical Center
Melanoma Oncology

Disclosures

None

Only FDA-approved immunotherapy regimens for the treatment of melanoma will be discussed in this presentation

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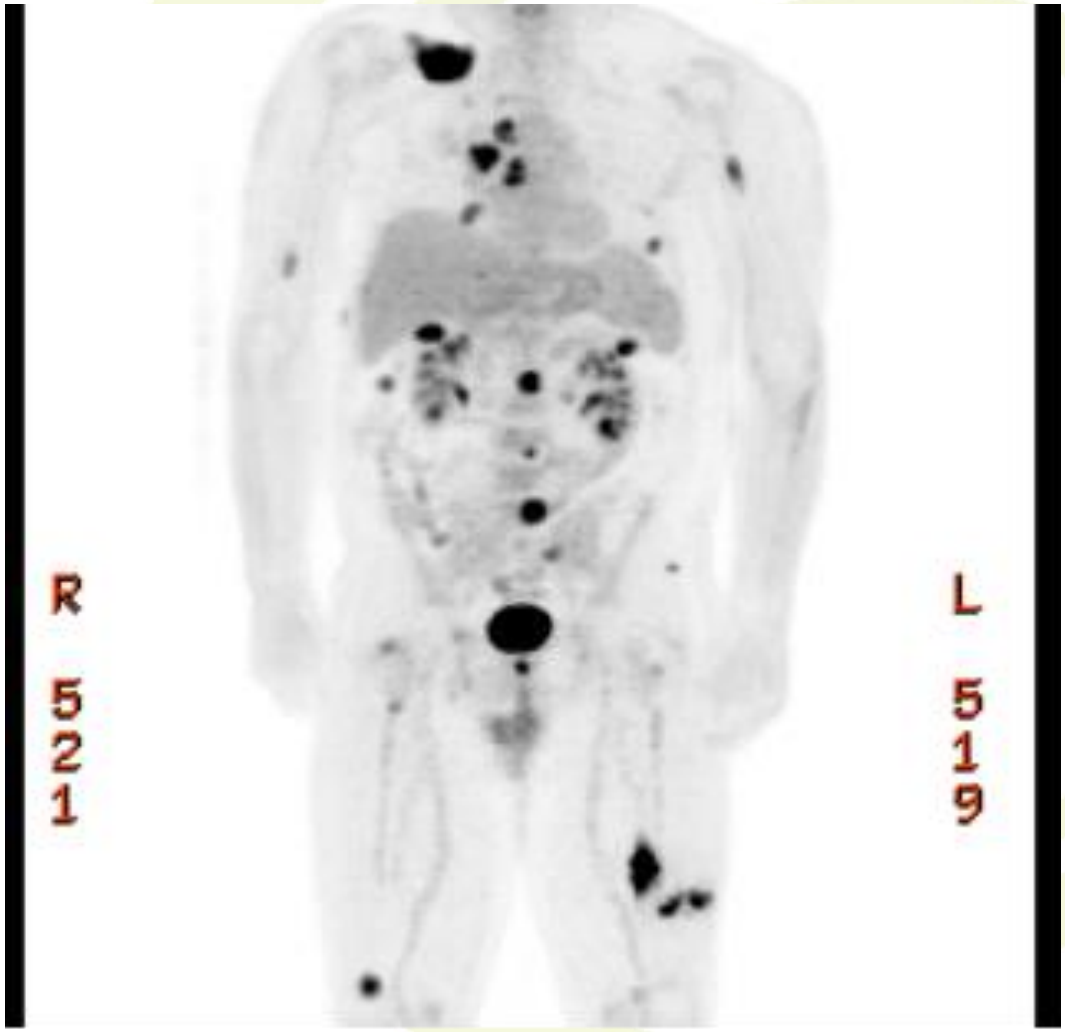
Before Treatment



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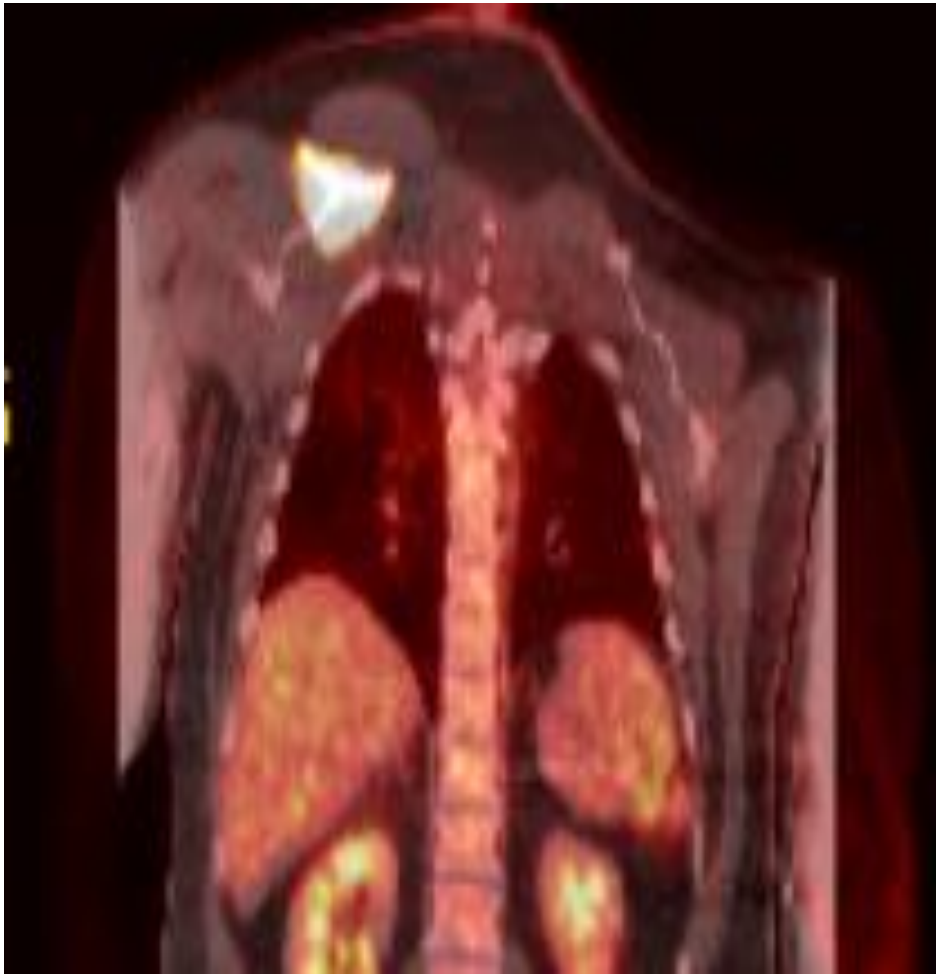
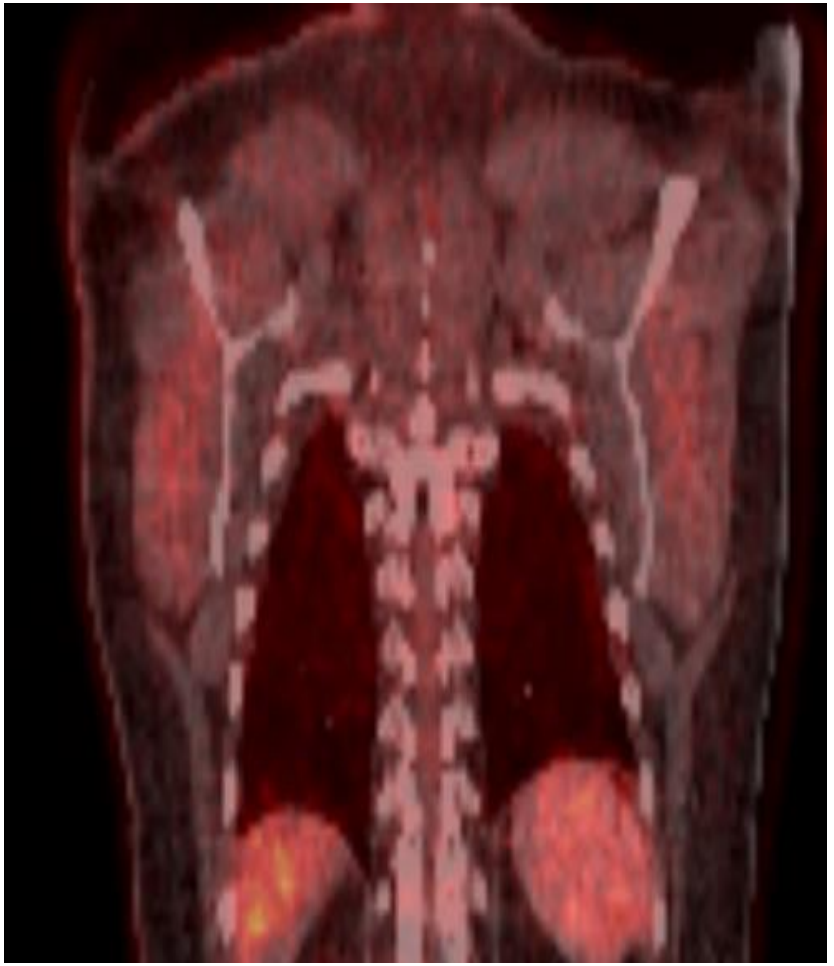
Before



After



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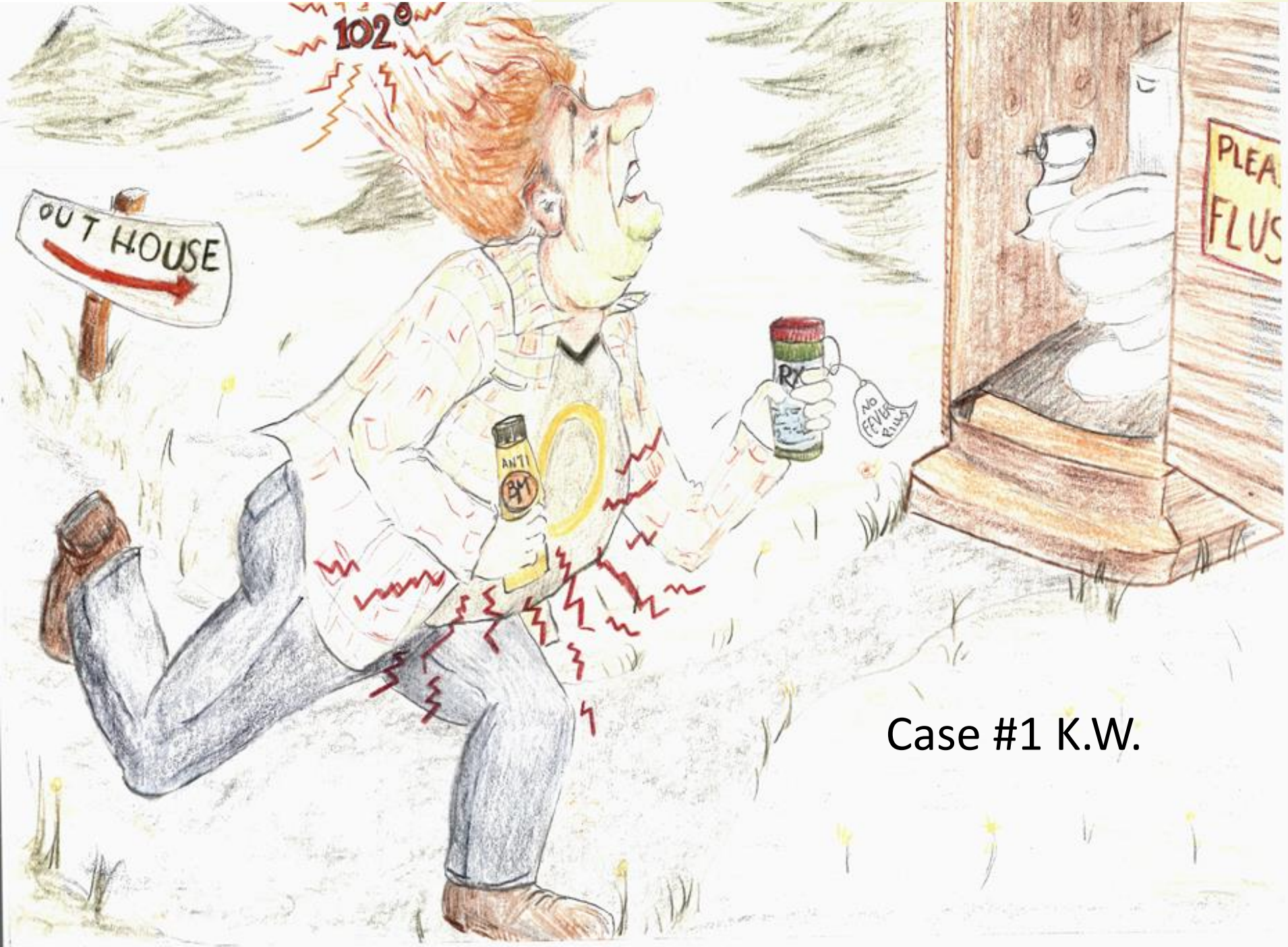
Oregon



Case #1 K.W.

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Choose the answer that is most correct

A.) Test for C-diff, draw blood & urine cultures, administer broad spectrum antibiotics

B.) Infectious workup, give IV hydration plus high dose IV & oral steroids

C.) Obtain CTs of the abdomen/pelvis & review labs for signs of neutropenia

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Case #2: S.R.

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Choose the answer that is most correct

A.) Recommend OTC antihistamines and lab draw: TSH, Cortisol & Metabolic Comp

B.) Request Rx of prednisone 1 mg/kg & an order for a CBC, tell patient that her next IT infusion will likely be held

C.) Advise patient to come to clinic as the rash could spread to her neck, face and mucosal membranes leading to airway closure. Possible admission for IV steroids

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Immunotherapy (IT) for Unresectable & Stage IV Melanoma

- **Ipilimumab**
- **Pembrolizumab**
- **Nivolumab**
- **Ipilimumab + Nivolumab** (ipi-nivo)

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Adjuvant Therapy

Interferon alpha

- Rarely used due to toxicity, length of therapy & efficacy

High-dose ipilimumab

- High-dose = high risk for serious AEs, some permanent

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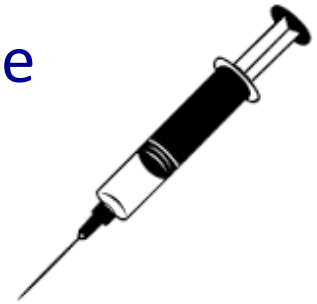
Other Tx Options

IL-2 (interleukin 2)

- Highly toxic
- Requires ICU stay
- Fairly obsolete due to newer IT options

TVEC Tamilogene laherparepvec



- Recently FDA approved
- Intralesional injection of live herpes virus

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Immunotherapy is not Chemotherapy

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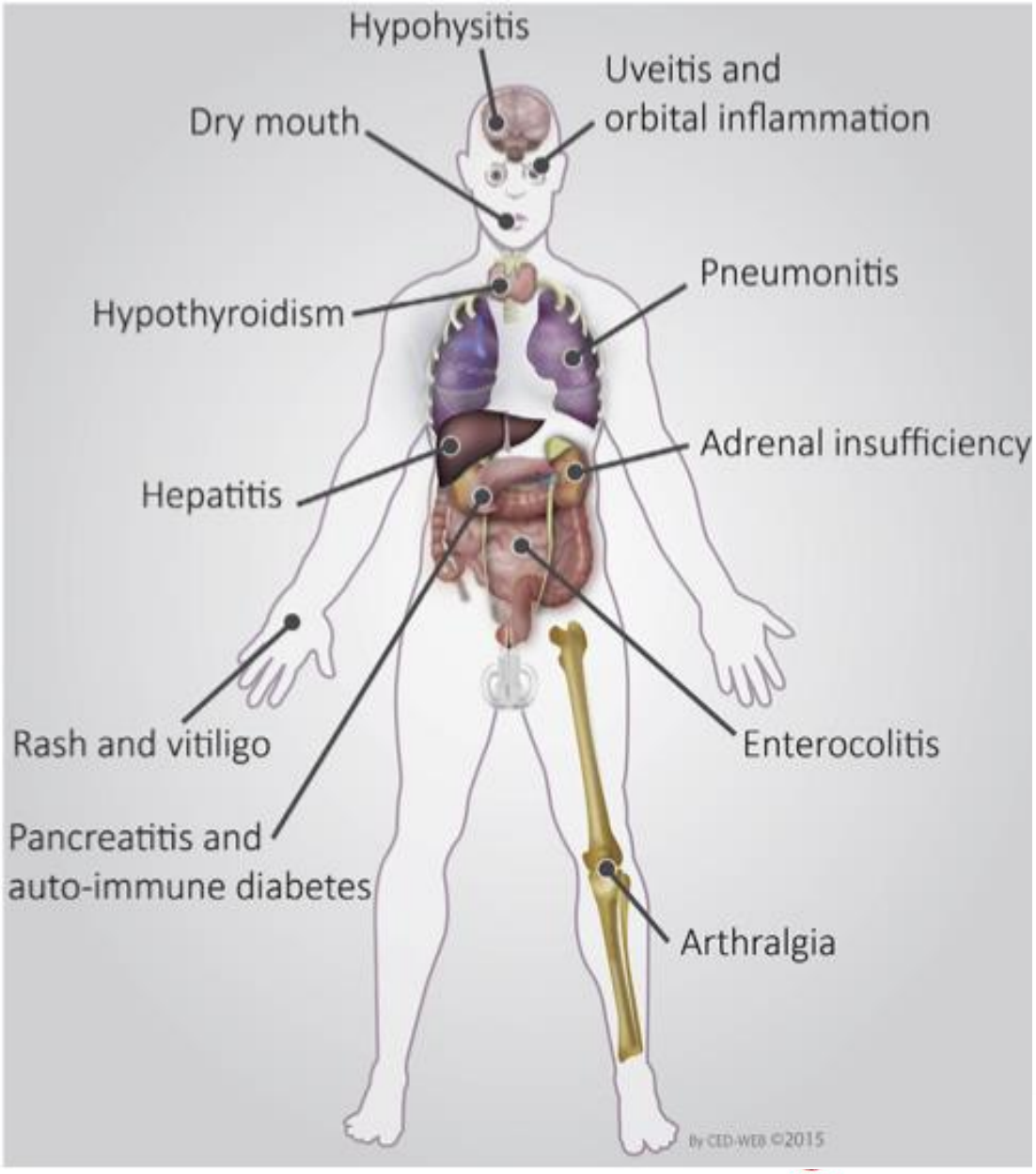
Targets of AEs



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Common AEs

- Fatigue
- Dermatitis: rash, itch
- Arthralgias
- Hypothyroidism
- **Diarrhea**
- Fever (ipi-nivo)

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Less Common AEs

- Hyperthyroidism
- Dry Mouth
- Vitiligo
- Constipation

- Loss of appetite
- N/V often assoc w/ grade 3-4 rxns
- Headaches – r/o brain mets, pituitary inflammation

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Rare + Serious AEs

Rare

- Guillain-Barre' Syndrome
- Myocarditis
- Neutropenia
- Ocular issues, i.e. uveitis
- Encephalitis
- Stevens-Johnson Syndrome
- Nephritis

Serious

(If grade 3-4, likely DC tx)

- **Colitis** (possible bowel perforation)
- **Hepatitis** (Possible N/V)
- **Pneumonitis** (SOB, dry cough, low O2 sats)
- **Diabetes** (the 3 Ps)

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Immunosuppression

- **Steroids –** the Key to Tx of most IT-related AEs
  - IV, oral, high dose, month or longer taper
  - Lower dose, long-term for some endocrinopathies
  - Monitor/educate patients on potential steroid AEs

- **Infliximab** (TNF alpha inhib) for refractory colitis

- **Mycophenalate** for refractory hepatitis

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Corticosteroid Management

& TNF alpha inhibitors

- **Prednisone** up to 1-2 mg/kg
- **Methylprednisolone** IV 125 mg X 1
- **Infliximab** 5 mg/kg q 2 weeks; can reactivate TB, so check PPD or Quantiferon

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Corticosteroid Management

- **Budesonide** 3-9 mg daily for mild colitis; provider preference, lacking good data
- **Topical steroids** for itch/rash, i.e. triamcinolone, hydrocortisone
- **Hydrocortisone** for hypophysitis & adrenal insufficiency, i.e. Hydrocortisone 15 mg a.m., 10 mg p.m.
- **Lengthy Steroid Tapers** (1 month +) or risk rebound sx

Hormone Supplement

- **Diabetes** = insulin, other glucose control meds
- **Hypophysitis & Adrenal insufficiency** = hydrocortisone
- **Thyroid** = levothyroxine, beta blocker or sx mgmt

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Endocrine Damage Hormone Supplement

Ailment	*Labs/Test*	*Tx*
• **Hypothyroid**	• **TSH (free T3 & T4)**	• **Levothyroxine**
• **Hyperthyroid**	• **TSH**	• **Beta blocker** (sx mgmt)
• **Adrenal insufficiency**	• **Cortisol, ACTH, check for hypotension**	• **Hydrocortisone**
• **Hypophysitis**	• **Brain MRI, a.m. Cortisol**	• **Hydrocortisone**
• **Diabetes**	• **Glucose, HgA1C**	• **Insulin, glucose control meds**

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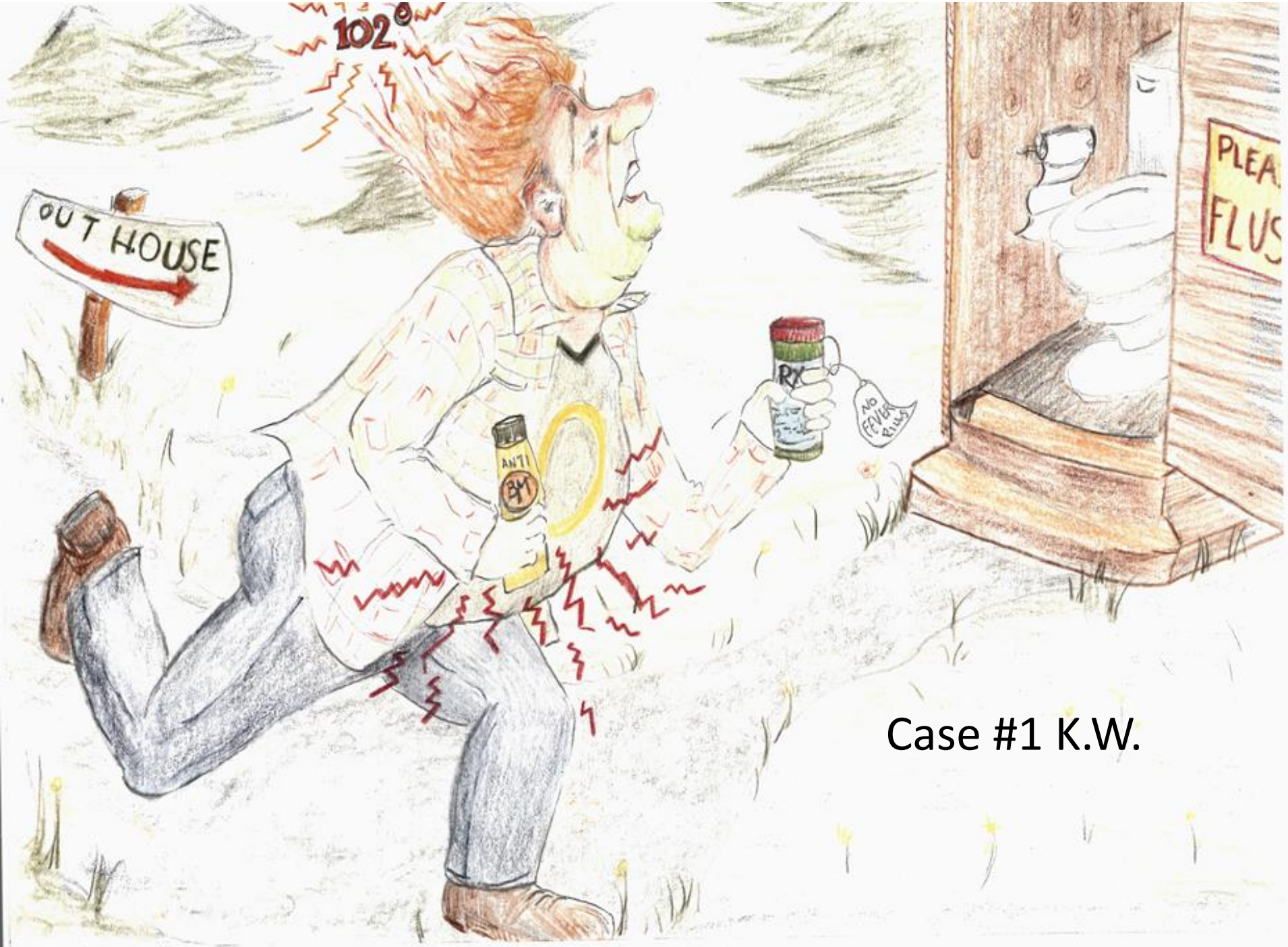
To Treat or Not to Treat

- **Continue Tx** for mild to moderate AEs
- **Grade 2 –** usually requires IT hold, tx symptoms with steroids &/or give hormone supplement PRN
- **Hold Tx for grade 3-4 AEs**: colitis, hepatitis, DM, pneumonitis,…
- **Endocrine issues** – tx depends on severity, give hormone supplement, likely long-term, anticipate them if giving combo ipi-nivo
- **Grading AEs: CTCAE = *common terminology criteria for adverse events***
  Follow your institution guidelines for managing AEs



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Case Study: K.W.

We consulted with the local ER attending physician and recommended the following:

- IV Solumedrol at 125mg IV X 1
- Oral steroids at 1 mg/kg = 150 mg
- Hydration and electrolyte replacement
- Metabolic comp, CBC
- Blood Cultures
- Guaiac stool and r/o C diff

The local MD, unfamiliar with IT AEs, would only initially agree to give 10 mg of prednisone & wait for culture results

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Case #2: S.R.

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Choose the answer that is most correct

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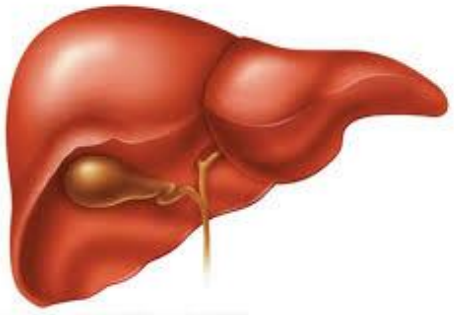
Case #3: H.G.

1 week after cycle #4 of ipi-nivo:

- **ALT 718, AST 452**
- **Glucose > 500**
- **TSH 88.6**
- **Cortisol < 1**
- Reported: severe arthralgias, fatigue, dehydration & other diabetic symptoms

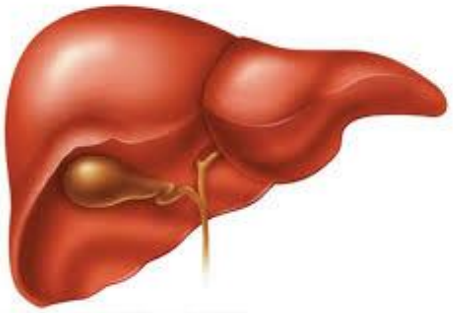


Case #3: H.G.

Diabetes:
- Referral to Endocrinology & Dietician
- Now on Lantus 14u and Humalog SS
- DM poorly controlled, BS averaging in the 300s

Elevated LFTs:
- Responded rapidly to 60 mg of steroids, months long taper, now on 5 mg prednisone daily. ALT 25, AST 24

Hypothyroid:
- 150 mcg levothyroxine daily. TSH 0.47



Adrenal Insufficiency:
- Controlled , fatigue mild, BP WNL. No recent cortisol level
- Hydrocortisone 15 mg a.m., 10 mg p.m.

Melanoma:
- Sep '16 PET/CT modest improvement, Jan '17 stable disease
- 10/21/16 restarted Nivo, now s/p 14 cycles

Take Home Points

- **Immunotherapy has a very long half-life**
- **Delayed onset** - AEs can occur weeks/months into or after tx
- **Report AEs at onset**
- **Risk of AEs higher** with **Ipilimumab** & combo **Ipi-Nivo**
- **Monitor Labs**:
  - ✓LFTs/metabolic comp
  - ✓ Endocrine: Glucose, TSH, ACTH + Cortisol if excess fatigue, ↓BP
  - ✓CBC (yes, but less concerning)
- **Screen:** Autoimmune dz & TB; PPD/Quantiferon prior to infliximab

Take Home Points

- **Review CTCAE** grading criteria & follow your institution guidelines for AE management
- **Continue Tx** for moderate AEs
- **Hold or DC Tx** for serious grade 3-4
- **Endocrine Damage** – long-term tx
- **Steroids** - high dose, lengthy taper!

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Any Questions?

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