# GESTION DE LA TOXICITÉ DES IMMUNOTHÉRAPIES

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GUSTAVE ROUSSY
CANCER CAMPUS
GRAND PARIS

DITEP
Drug Development Department

# DISCLOSURE INFORMATION

## Stephane CHAMPIAT

Honoraria from Amgen, AstraZeneca, BMS, Janssen, MSD, Novartis and Roche.

As part of Gustave Roussy Drug Development Department (DITEP):

- Sub-Investigator of Clinical Trials for Abbvie, Agios Pharmaceuticals, Amgen, Argen-X Bvba, Arno Therapeutics, Astex Pharmaceuticals, Astra Zeneca, Aveo, Bayer Healthcare Ag, Bbb Technologies Bv, Blueprint Medicines, Boehringer Ingelheim, Bristol Myers Squibb, Celgene Corporation, Chugai Pharmaceutical Co., Clovis Oncology, Daiichi Sankyo, Debiopharm S.A., Eisai, Eli Lilly, Exelixis, Forma, Gamamabs, Genentech, Inc., Glaxosmithkline, H3 Biomedicine, Inc, Hoffmann La Roche Ag, Innate Pharma, Iris Servier, Janssen Cilag, Kyowa Kirin Pharm. Dev., Inc., Loxo Oncology, Lytix Biopharma As, Medimmune, Menarini Ricerche, Merck Sharp & Dohme Chibret, Merrimack Pharmaceuticals, Merus, Millennium Pharmaceuticals, Nanobiotix, Nektar Therapeutics, Novartis Pharma, Octimet Oncology Nv, Oncoethix, Onyx Therapeutics, Orion Pharma, Oryzon Genomics, Pfizer, Pharma Mar, Pierre Fabre, Roche, Sanofi Aventis, Taiho Pharma, Tesaro, Inc, Xencor
- Research Grants from Astrazeneca, BMS, Boehringer Ingelheim, Janssen Cilag, Merck, Novartis, Pfizer, Roche, Sanofi
- Non-financial support (drug supplied) from Astrazeneca, Bayer, BMS, Boringher Ingelheim, Johnson & Johnson, Lilly, Medimmune, Merck, NH TherAGuiX, Pfizer, Roche

# Anti PD-1 vs chemotherapy

Nivolumab vs docetaxel in NSCLC

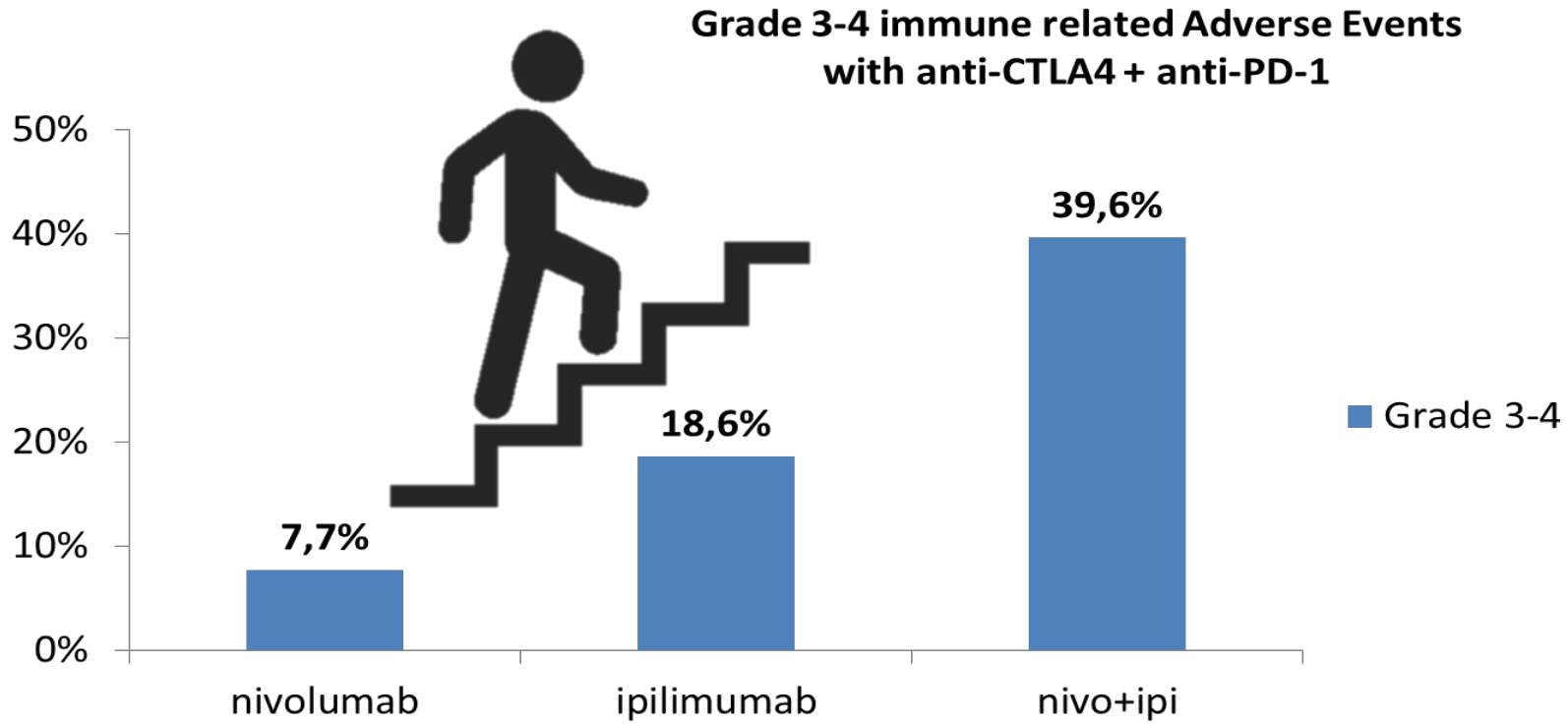
| | Nivolumab n = 287 | Docetaxel n = 268 |
|---|---|---|
| All Grade AEs, any cause | 98% | 99% |
| Treatment-related AEs | 69% | 88% |
| Grade 3-4 AEs, any cause | 46% | 67% |
| Treatment-related Grade 3-4 AEs | 10% | 54% |
| Grade 5 AEs, any cause | 8% | 5% |
| Patients withdrawing from treatment due to AEs | 5% | 15% |

Treatment-related Grade 5 events

- Nivolumab (n = 1): encephalitis (causality was changed after the database lock)
- Docetaxel (n = 1): febrile neutropenia

Borghaei et al. (2015). Nivolumab versus Docetaxel in Advanced Nonsquamous Non–Small-Cell Lung Cancer. *NEJM*

# irAEs are NOT so rare when used in combination




Larkin et al, N Engl J Med 2015.

# It’s not about the frequency…**it’s about diversity !**

# It’s not about the frequency…**it’s about diversity !**

**REPIRATORY**
Pneumonitis
Pleuritis
Sarcoid-like granulomatosis

**EYE**
Uveitis
Conjunctivitis
Scleritis, episcleritis
Blepharitis
Retinitis

**ENDOCRINE**
Hyper or hypothyroidism
Hypophysitis
Adrenal insufficiency
Diabetes

**CARDIO VASCULAR**
Myocarditis
Pericarditis
Vasculitis

- New
- Diverse
-Uncommon

**GASTRO INTESTINAL**
Colitis
Ileitis
Pancreatitis
Gastritis

**RENAL**
Nephritis

**LIVER**
Hepatitis

**NEUROLOGIC**
Neuropathy
Guillain Barré
Myelopathy
Meningitis
Encephalitis
Myasthenia

**SKIN**
Rash
Pruritus
Psoriasis
Vitiligo
DRESS
Stevens Johnson

**BLOOD**
Hemolytic anemia
Thrombocytopenia
Neutropenia
Hemophilia

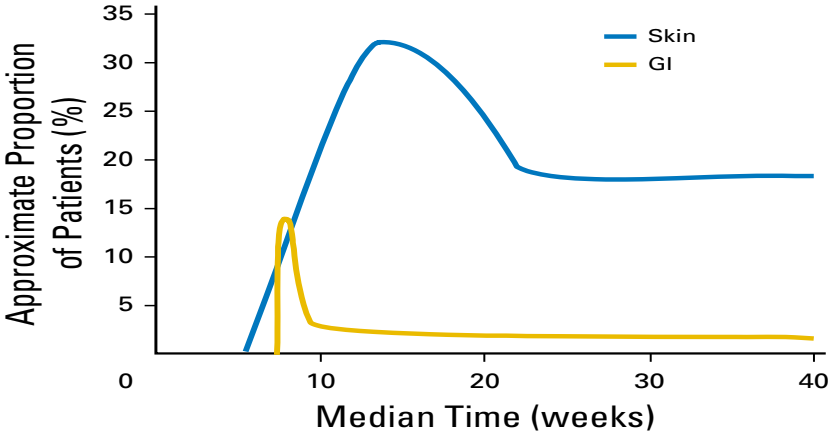
**MUSCULO SKELETAL**
Arthritis
Dermatomyositis

Champiat et al. (2016). Management of Immune Checkpoint Blockade Dysimmune Toxicities: a collaborative position paper. *Annals of Oncology*

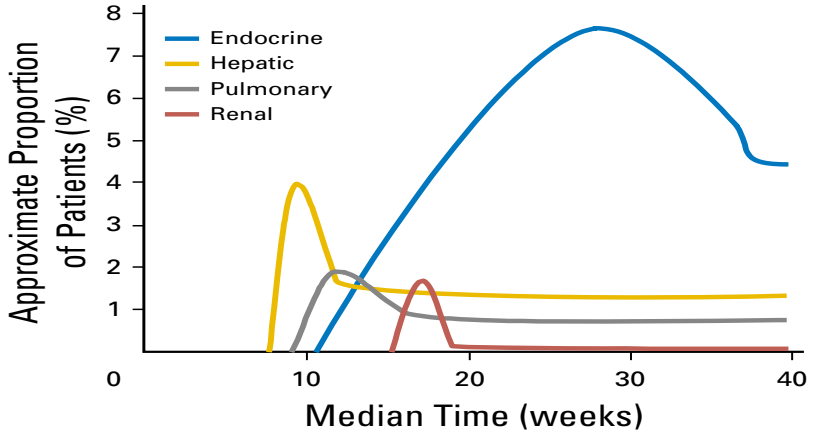
# Kinetics of onset and resolution of anti-PD1 irAEs

Safety Profile of Nivolumab Monotherapy:
A Pooled Analysis of Patients With Advanced Melanoma (N=576)
Weber et al. JCO 2016

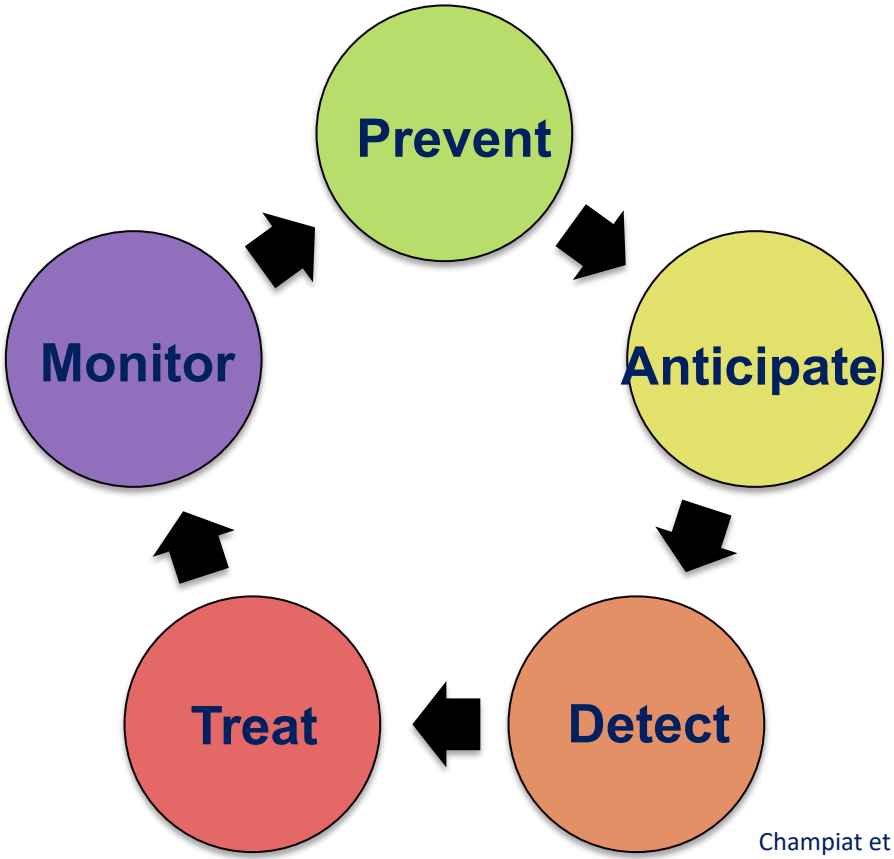
## Most common irAEs (≥ 10%)




## Less common irAEs (<10%)



# Immunotherapy toxicity management




Champiat et al. , Annals of Oncology, 2016

## Prevent

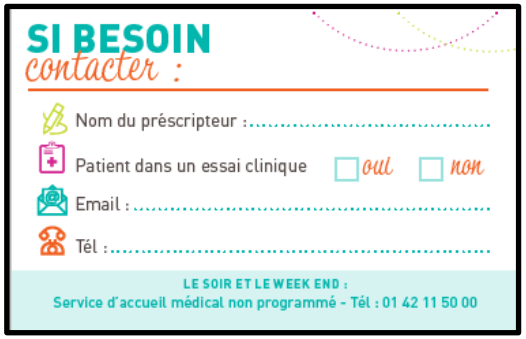
Inform patient
& the whole health care team

**Report quickly**
**any new, persitent or worsening of pre-existing symptom**

**Early recognition and management**
**may limit worsening or toxicity severity**

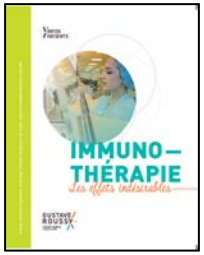
# Prevent

## Patient card





## Medical information letter




# Prevent

**Search for risk factors**

## Personal and family history

-autoimmune disease, systemic disease, chronic inflammatory disease

(Crohn's disease, arthritis, lupus, ...)

-previous immunotherapy toxicity

-chronic respiratory, cardiovascular, liver pathologies...

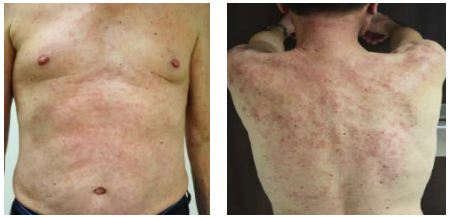
-recent severe infections, chronic viral infections

# Prevent

## Most frequent irAEs

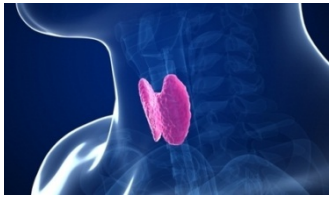
**Fatigue**
***20%***

**Rash**
***15%***

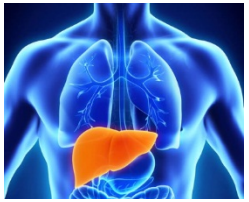


**Diarrhea**
***10-15%***

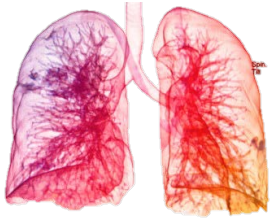
**Hypothyroidism**
***5-10%***



**Hepatic**
***5%***



**Pneumonitis**
***<5%***

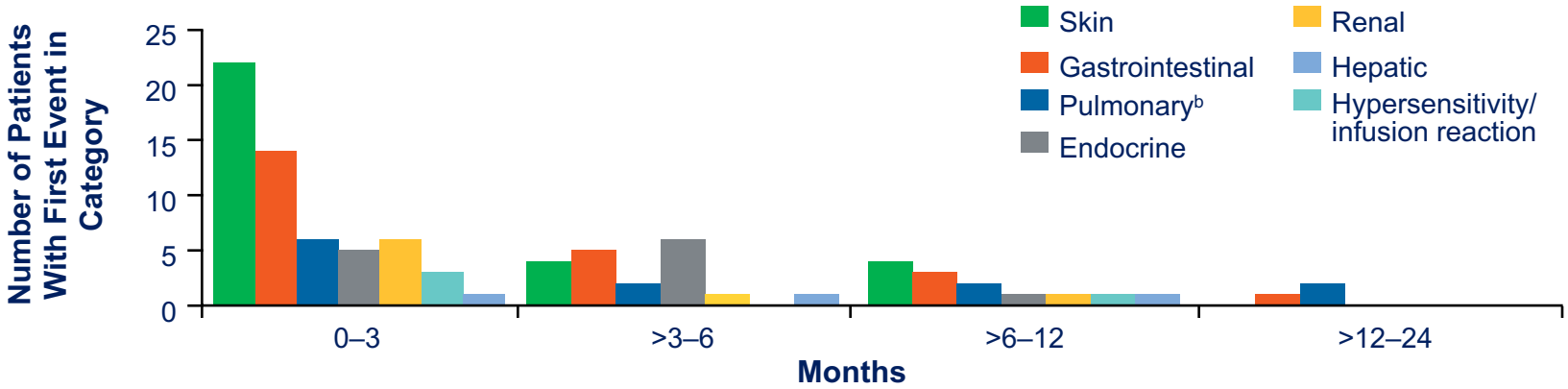


*Adapted from Boutros C et al. Nature Reviews Clinical Oncology CR 2016*

Prevent

# Time to onset of Treatment-related select AE

## Example: Nivolumab in SCC (pooled analysis from CM-063 & CM-017)




| | | | | |
|---|---|---|---|---|
| **Pts still on study, n** | 248 | 206 | 153 | 84 |
| **Pts still on treatment, n** | 248 | 134 | 85 | 38 |
| **Total pts with a first event,[a] n** | 49 | 14 | 10 | 2 |

Antonia S, ESMO 2015, abstract: 346

# Anticipate

Baseline check-up is KEY

**Physical exam**

-Performance status, Weight, size

-Heart rate and blood pressure, **baseline electrocardiogram**

-**Pre-existing symptoms** :

- ✔Bowel transit
- ✔ Rash
- ✔ Signs of motor or sensory neuropathy
- ✔ Dyspnea and coughing
- ✔ Arthralgia

-History of fever or recent infection

-Ongoing treatment

# Anticipate

## Anticipating by starting on a strong and adjusted check-up

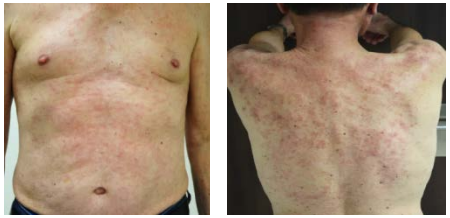
| | | Baseline | Every cycle |
|---|---|---|---|
| General | Complete CBC<br>Serum electrolytes, creatininemia<br>Liver tests | x | x |
| | Haemostasis<br>CK tests<br>Lipase<br>CRP | x | |
| Endocrine | TSH, T4, T3 | x | Every 2 cycles |
| | Cortisolemia/ACTH 8h<br>FSH, LH, oestradiol/testosterone<br>IGF1, Prolactine<br>Ab anti-îlots β, anti-insulin, anti-GAD | for IO-IO combination or adjuvant or neoadjuvant setting | |
| Urine | Urine dipstick | x | |
| Infectious | Virology: HIV, HCV, HBV serologies<br>Quantiferon tuberculosis (a) | x | |
| Cardiac | ECG<br>BNP and troponin | x | During the first 3 months |
| Respiratory | Thoracic CT imaging | x | |

# Detect

## Most frequent irAEs

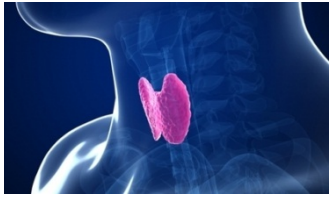
**Fatigue**
***20%***

**Rash**
***15%***

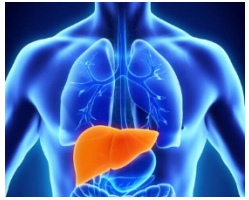


**Diarrhea**
***10-15%***

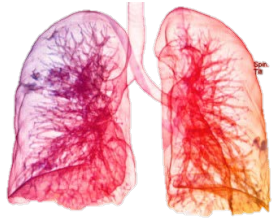
**Hypothyroidism**
***5-10%***



**Hepatic**
***5%***



**Pneumonitis**
***<5%***

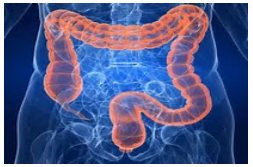


*Adapted from Boutros C et al. Nature Reviews Clinical Oncology CR 2016*

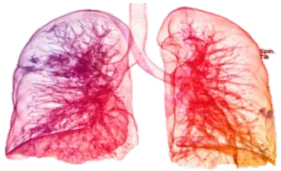
Detect

# Life threatening irAEs

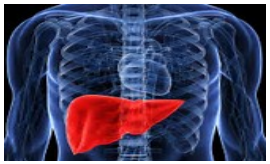
**1 - 5 %**



**GI**
Colitis



**Lung**
Pneumonitis
Pleural/pericardic effusion



**Liver**
Hepatitis

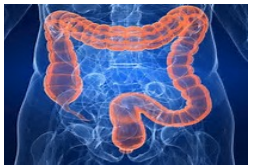
**Mostly reversible upon immunotherapy discontinuation**
**+/- corticosteroids**

**Boutros C et al. Nature Reviews Clinical Oncology CR 2016**

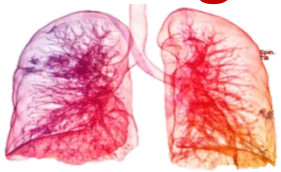
# Detect

## Life threatening irAEs

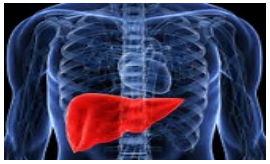
**1 - 5 %**



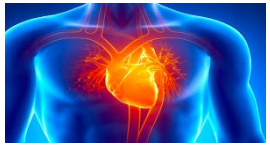
**GI**
Colitis



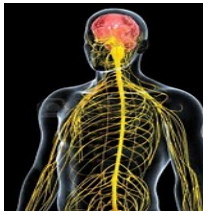
**Lung**
Pneumonitis
Pleural/pericardic effusion



**Liver**
Hepatitis



**Cardiac**
Myocarditis

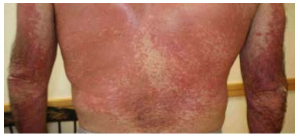


**Neurological**
Guillain Barré
Encephalitis
Myelitis

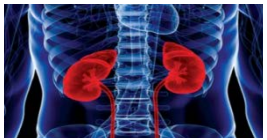
**< 1 %**

**Endocrine**
Adrenal insufficiency
Fulminant diabetes

**Hematological**
Anemia
Thombopenia
Neutropenia



**Skin**
DRESS
Steven Johnson



**Renal**
Nephritis

# Incidence and Types of Immune Checkpoint Inhibitor-Related Fatalities From Systematic Review and Meta-analysis

| Variable | Anti-CTLA-4 (n = 5368) | Anti-PD-1 (n = 9136) | Anti-PD-L1 (n = 3164) | Anti-PD-1/PD-L1 Plus CTLA-4 (n = 1549) |
|---|---|---|---|---|
| Deaths, No. (%) | 58 (1.08) | 33 (0.36) | 12 (0.38) | 19 (1.23) |
| Type of fatal toxic effect | | | | |
| Colitis | 23 (40) | 2 (6) | 0 | 2 (11) |
| Pneumonitis | 3 (5) | 14 (42) | 5 (42) | 4 (21) |
| Hepatitis | 5 (9) | 0 | 1 (8) | 2 (11) |
| Cardiac | 9 (16) | 4 (12) | 3 (25) | 4 (21) |
| Neurologic | 1 (2) | 1 (3) | 0 | 3 (16) |
| Nephritis | 1 (2) | 0 | 0 | 1 (5) |
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| Hemorrhagic/thrombotic | 2 (4) | 1 (3) | 0 | 1 (5) |
| Electrolyte imbalance | 1 (2) | 2 (6) | 0 | 0 |
| Multiorgan failure | 3 (5) | 0 | 0 | 0 |
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Wang et al. JAMA Oncology 2018

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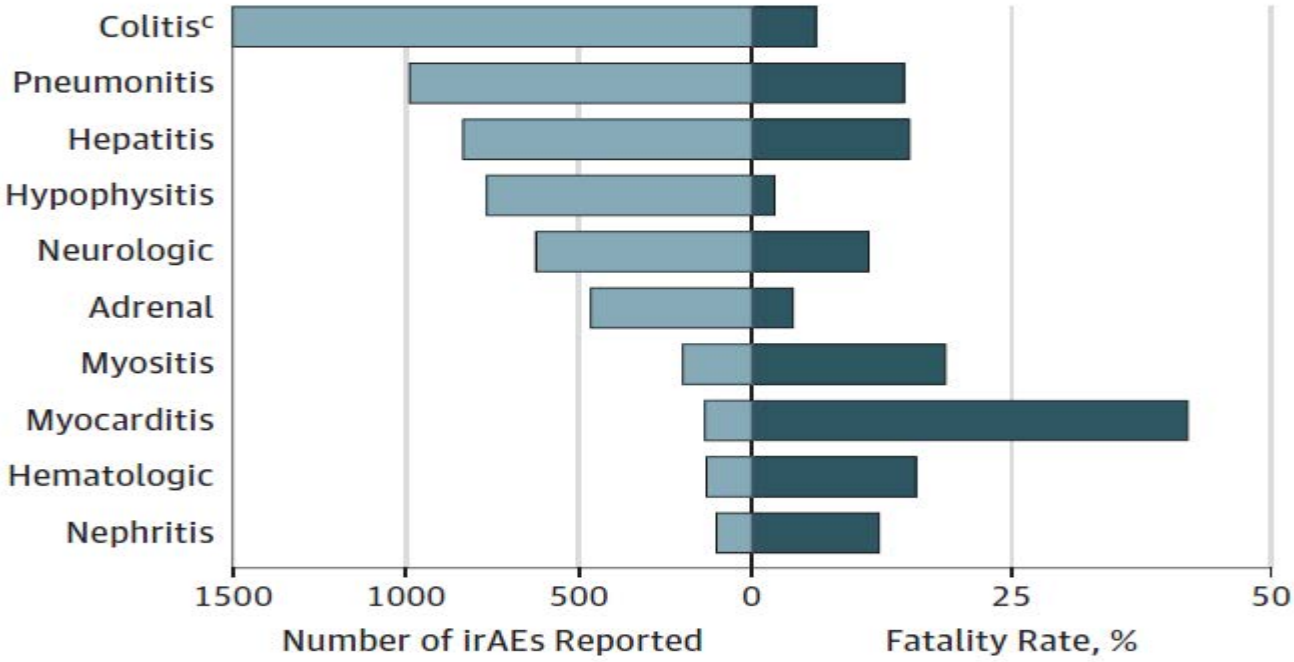
Wang et al. JAMA Oncology 2018

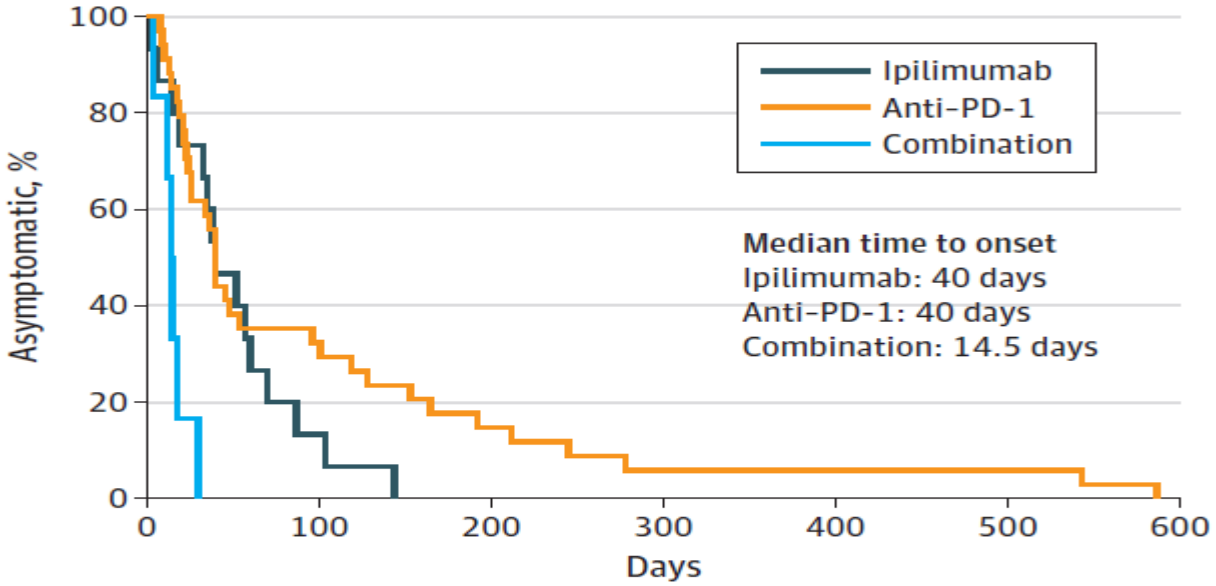
**Number of cases and fatality rate for each class of toxic effect**




Wang et al. JAMA Oncology 2018

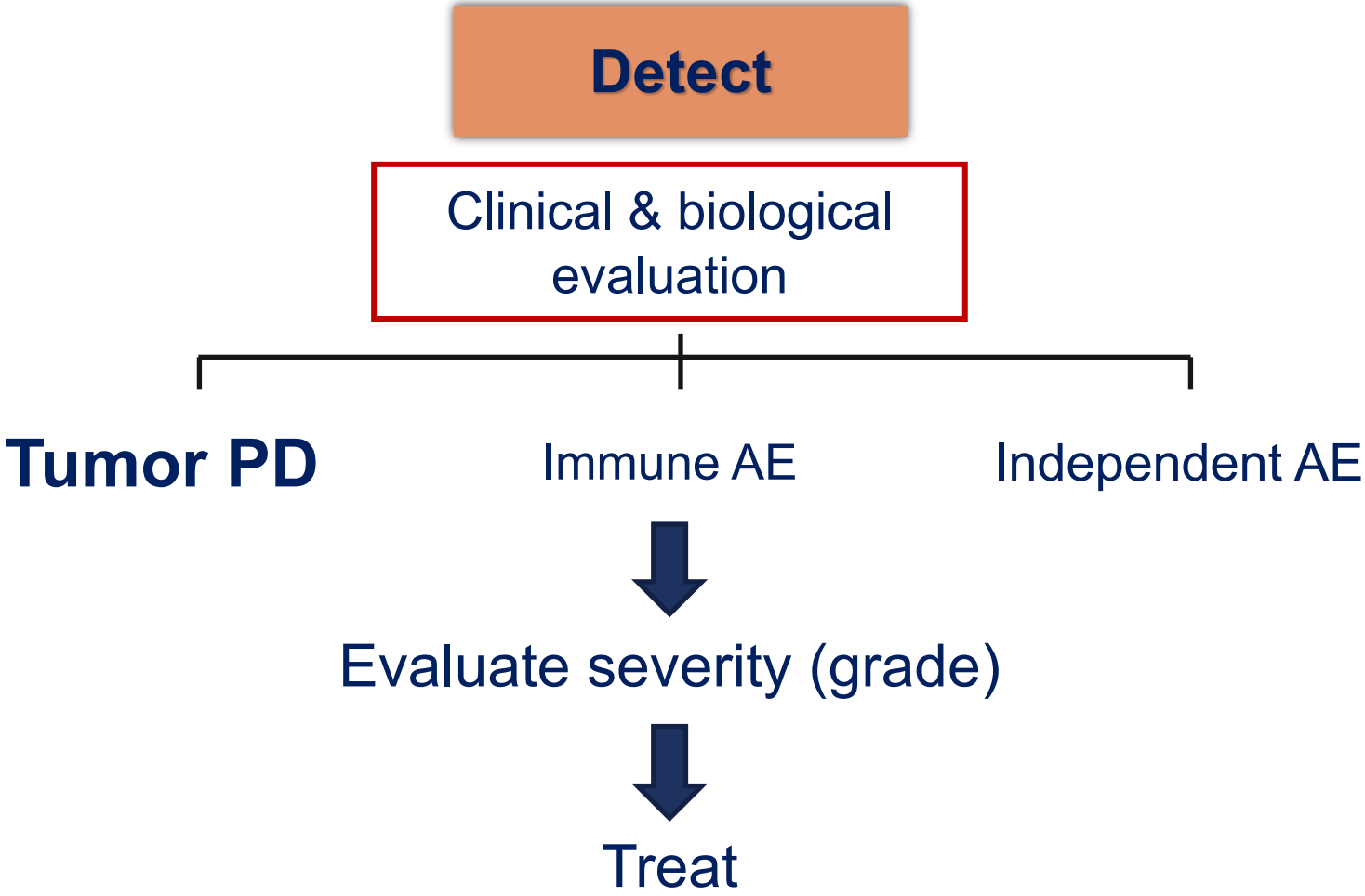
# Detect

## Time to Symptom Onset of Fatal Toxic Effects by ICI Regimen




| No. at risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Ipilimumab | 15 | 2 | 0 | 0 | 0 | 0 | 0 |
| Anti-PD-1 | 34 | 11 | 5 | 2 | 2 | 2 | 0 |
| Combination | 6 | 0 | 0 | 0 | 0 | 0 | 0 |

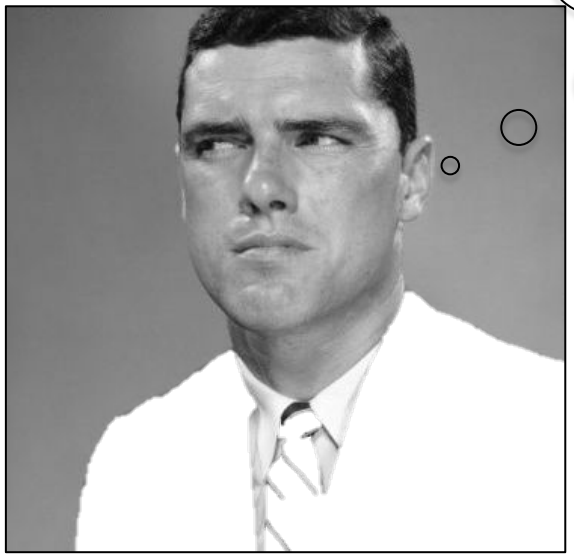
Wang et al. JAMA Oncology 2018


Detect
Clinical & biological evaluation
Tumor PD
Immune AE
Independent AE
Evaluate severity (grade)
Treat

# *In case of immunity-related toxicity*

**Have the corticosteroid reflex !**

**We think about it too late**
**...We stop them too soon**



## ☑ Differential diagnostics?

Infectious+++

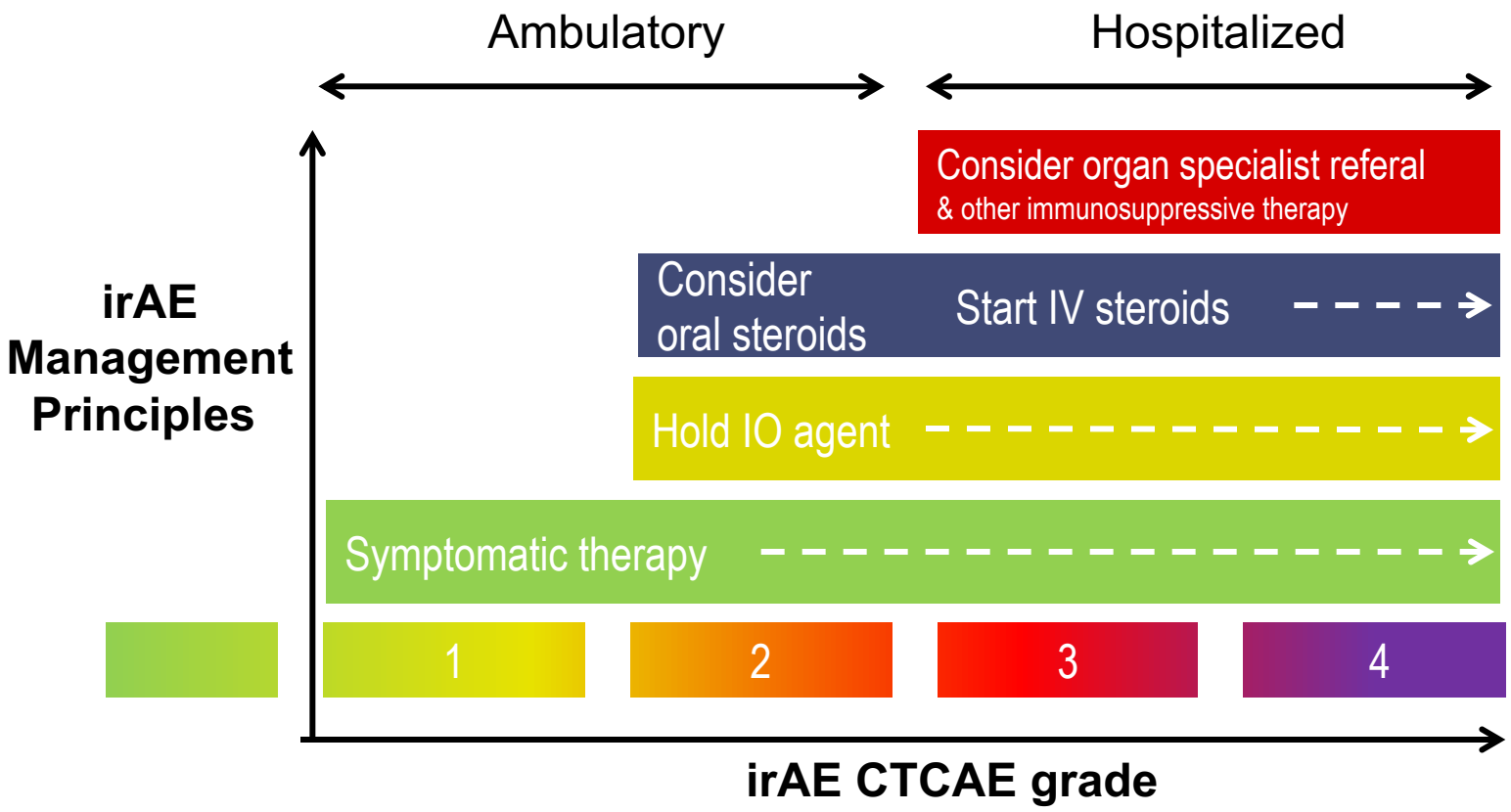
## ☑ Severity ?

If severe, do not delay steroid therapy

## ☑ Specialized referral ?

Complex pathology, other immunosuppressive therapy

# General management strategies for irAEs



# Treat

## Key points

- Close monitoring
- Patient information
- Symptomatic treatment
- Suspension of immunotherapy or permanent discontinuation
- Discuss corticosteroid therapy
- Specialized referral
- Other immunosuppressive therapy

# Treat

**Corticosteroids**

***We think about it too late***

***We stop them too soon***

- **Before initiation: eliminate an infection**
- **Antibio-prophylaxis: oral trimethoprim/sulfamethoxazole**
- **Progressive tapering: ≥ 1 month**

# Treat

## Immunotherapy management

**> Suspend +/- Resume when irAE returns to Grade 0-1**

**> Stop definitively for**

**any life threatening irAE**

**inability to reduce corticosteroid therapy**

**Persistent grade 2 or 3**

**Any severe toxicity or grade 3 that recurs**

# Treat

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

*Annals of Oncology* 28 (Supplement 4): iv119–iv142, 2017
doi:10.1093/annonc/mdx225

CLINICAL PRACTICE GUIDELINES

## Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

J. B. A. G. Haanen[1], F. Carbonnel[2], C. Robert[3], K. M. Kerr[4], S. Peters[5], J. Larkin[6] & K. Jordan[7], on behalf of the ESMO Guidelines Committee*

Puzanov et al. Journal for ImmunoTherapy of Cancer (2017) 5:95
DOI 10.1186/s40425-017-0300-z

Journal for ImmunoTherapy of Cancer

POSITION ARTICLE AND GUIDELINES Open Access

## Managing toxicities associated with immune checkpoint inhibitors: consensus recommendations from the Society for Immunotherapy of Cancer (SITC) Toxicity Management Working Group

I. Puzanov[11], A. Diab[21], K. Abdallah[3], C. O. Bingham III[4], C. Brogdon[5], R. Dadu[2], L. Hamad[1], S. Kim[2], M. E. Lacouture[6], N. R. LeBoeuf[7], D. Lenihan[8], C. Onofrei[9], V. Shannon[2], R. Sharma[1], A. W. Silk[12], D. Skondra[10], M. E. Suarez-Almazor[2], Y. Wang[2], K. Wiley[11], H. L. Kaufman[12†], M. S. Ernstoff[11*†] and on behalf of the Society for Immunotherapy of Cancer Toxicity Management Working Group

JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

## Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline

*Julie R. Brahmer, Christina Lacchetti, Bryan J. Schneider, Michael B. Atkins, Kelly J. Brassil, Jeffrey M. Caterino, Ian Chau, Marc S. Ernstoff, Jennifer M. Gardner, Pamela Ginex, Sigrun Hallmeyer, Jennifer Holter Chakrabarty, Natasha B. Leighl, Jennifer S. Mammen, David F. McDermott, Aung Naing, Loretta J. Nastoupil, Tanyanika Phillips, Laura D. Porter, Igor Puzanov, Cristina A. Reichner, Bianca D. Santomasso, Carole Seigel, Alexander Spira, Maria E. Suarez-Almazor, Yinghong Wang, Jeffrey S. Weber, Jedd D. Wolchok, and John A. Thompson in*

# Skin reactions

**Topical emollients**,
avoid skin irritants
avoid sun exposure

**Consider dermatology referral** and skin biopsy

Urgent **dermatologist referral**
**IV steroids** 1-2 mg/kg

**Topical steroids**
+/- **antihistamines**
for pruritis

**Withhold ICI**
**Initiate systemic steroids**
0,5 – 1 mg/kg

**Severity**

Fever > 39° c
Mucosal involvement
Ulcerations / rash infiltration
Epidermal detachment
Rash diffusion rate
Bullous eruptions
No prompt resolution under corticosteroids
DRESS /Stevens Johnson

# Hypothyroidism


**Repeat TSH, FT3/FT4**
**Next cycle**

**Hormone replacement therapy**
L-thyroxine 1,5 ug/kg/day

***Start lower in elderly, cardiac history***

**Withhold ICI**

## Consider endocrinologist referral if :

- Ultrasound abnormalities (nodules)
- Autoantibodies positivity
- Treatment initiation in elderly pts, cardiac history pts

# Fatigue, asthenia

**Specify associated symptoms**

Dyspnea?
Muscular weakness ?
Muscle or joint pain?
Fatigability?
Psychomotor slowdown / confusion?

**Severity**

≥ ECOG score 3 -4
limited self-care, confined to bed or chair 50% or more of waking hours

## Minimal investigations

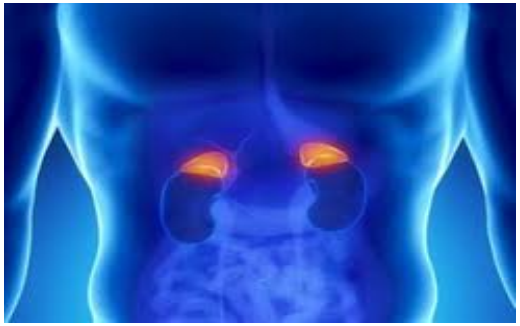
- **ECG, BNP, Troponin**
- **CBC**
- **Iono, Creatinine, Urine dipstick, calcium, glucose**
- **Liver tests**
- **CPK**
- **Endocrine : -morning cortisol**
  **-TSH T3/T4**

MEDICAL EMERGENCY

# Adrenal insufficiency

**Symptoms are NON-SPECIFIC**

asthenia, anorexia, orthostatic hypotension, abdominal pain, nausea, vomiting, hypoglycemia, hyponatremia



**Severity = ICU**

hypotension / hypovolemic shock
Abdominal pain, vomiting
Neurological Disorders
ECG: signs of hyperkalaemia

**Therapeutic emergency + + +**

**If suspected : do not wait for diagnosis : morning cortisol**

**start HYDROCORTISONE 100 mg IM / SC then 200 mg / 24h IVSE**

**and HYDRATION**

# Diarrhea

Ambulatory ⟷ Hospitalisation

CBC, CRP
Iono, urea, creatinine
Liver tests
TSH FT3/FT4
Stool culture,
Clostridium difficile toxin

If colitis Sx :
**Abdominal CT-scan**

Urgent **Gastroenterologist referral**

**Symptomatic Mx**
Oral fluids, loperamide, avoid high fibre/lactose diet

**Withhold ICI**

Persistent G2 or G3-4 :
**Sigmoido/colonoscopy +biopsies**


**Oral steroids 0,5-1mg/kg**
Do not wait for sigmoidoscopy/colonoscopy to start

**IV steroids 1-2 mg/kg**

**Infliximab**
If no improvement in 72h or worsening

**Grading**
- G1 : < 3 liquid stools /day over baseline, feeling well
- G2 : 4-6 liquid stools /day over baseline, abdominal pain or blood in stool
- G3/4 : > 6 liquid stools /day over baseline or patient feeling unwell

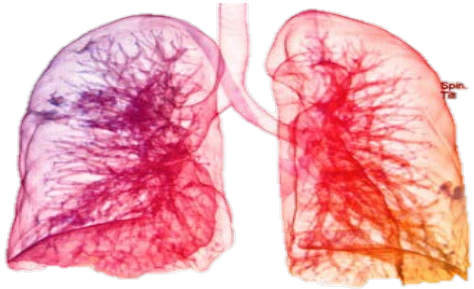
***Signs of bowel perforation :***
Defense, contracture
Sepsis : fever, tachycardia
Signs of shock
**= surgical referral**

# Inflammatory pneumonitis

## Signs and symptoms

Dry cough, progressive shortness of breath, tachypnea, hypoxia

**May be asymptomatic** with radiographic changes only



## Severity

- **Fever**
- **Chest pain**
- **Oxygen saturation < 90%**
- **Dyspnea at rest**
- **Acute respiratory distress**

## Differential diagnosis

- **Pulmonary embolism**
- **Tumor progression**
- **Infectious pneumonia, COPD decompensation**
- **Congestive heart failure**

- **Dysimmune toxicities :**
  - **Thoracic :** pleural effusion
  - **Cardiac :** pericarditis, myocarditis
  - **Neurologic :** myathenia, Guillain barré

=> **ECG , BNP, troponin**

# Inflammatory pneumonitis

Ambulatory ⟷ Hospitalisation

- **CBC, CRP**
- **Blood culture**
- Urinary tests for pneumococcus and legionella
- Consider sputum infection screening

**High resolution CT**
**Lung function tests**
Spirometry
DLCO

**Lung specialist referral**
**bronchoscopy + BAL**

**Asymptomatic**
**Radiologic changes**

**Surveillance**
Clinical (pulmonary function tests)
& Lung imaging

**Symptomatic**
**no oxygen needed**

**Withhold**
**ICI**
**Oral steroids**
**1 mg/kg**
If possible after BAL
**Discuss empiric antibiotics**
If suspicion of infection (fever, CRP, elevated neutrophils)

**Symptomatic**
**oxygen needed**

**Discuss ICU**

**IV steroids**
bolus then
**1-2 mg/kg**

**+ empiric antibiotics**

**Discuss cyclophosphamide**
If no improvement in 48h or worsening

# Hepatitis

Ambulatory ⟷ Hospitalisation in hepatology

**Liver function tests**
albumin
PT / INR /factor V

**Viral serologies**
A / B /C
PCR HEV, CMV

**Autoantibodies**
ANA/ SMA/LKM/LC1
Iron studies

**Hepatologist referral**
**+ liver biopsy**
If persistent grade 2
or grade 3-4

**Severity**
- **Coagulopathy :** PT, factor V < 50%
- **Encephalopathy**
- **Fever**
- **Bilirubin > 10 N**

**Hepatic imaging**

**Surveillance of liver FT**

**Withhold ICI**

**G1**
Avoid alcohol
Review hepatotoxic drugs/products

**G2**
**Steroids 1mg/kg**

**G3/4**
**IV steroids 1-2 mg/kg**

**Mycophenolate mofetil**
If no improvement in 72h
or worsening

| | Grade 1 | Grade 2 | Grade 3 | Grade 4 |
|---|---|---|---|---|
| ALT /AST | > ULN – 3 ULN | > 3 – 5 ULN | > 5 – 20 ULN | > 20 ULN |
| Bilirubin | > ULN – 1,5 ULN | > 1,5 – 3 ULN | > 3 – 10 ULN | > 10 ULN |
| GGT/ALP | > ULN – 2,5 ULN | > 2,5 – 5 ULN | > 5 – 20 ULN | > 20 ULN |

# Myositis

**Signs and symptoms**

Muscle pain
Muscle weakness
Muscle atrophy

**Diagnosis : elevated CK**

***Check for extra-articular symptoms:***

- Arthalgia
- Fever
- Rash
- Mouth ulcerations
- Dry syndrome
- …

**Severity**

- Swallowing disorder
- **Bronchial congestion**
- **Axial** involvement: muscles of the trunk and neck
- **Heart** involvement

⇒ **Look for myocarditis**

ECG, troponin, BNP

**Differential diagnosis**

- Local tumor invasion
- Denutrition
- Cortisone, statin myopathies
- Dysimmune toxicities :
  - Myathenia gravis
  - Thyroid dysfunction => TSH, FT4, FT3

⇒ **Look for associated myasthenia gravis**

Anti acetylcholine receptor Ab

**Discuss management with Internist**

# Myocarditis

**Signs and symptoms are non specific**

Fatigue, weakness
Oedema
Dyspnea
Palpitations
Chest pain
Hypotension
Fever

**Diagnosis**
**=**
**Therapeutic emergency :**

**Transfer to cardiology ICU**
(risk of rapid progression)

**High dose corticosteroids**

***If suspected :***

**ECG**
**Troponin**
**BNP**
**Discuss echocardiography**
**+/- heart MRI**

**Differential diagnosis**

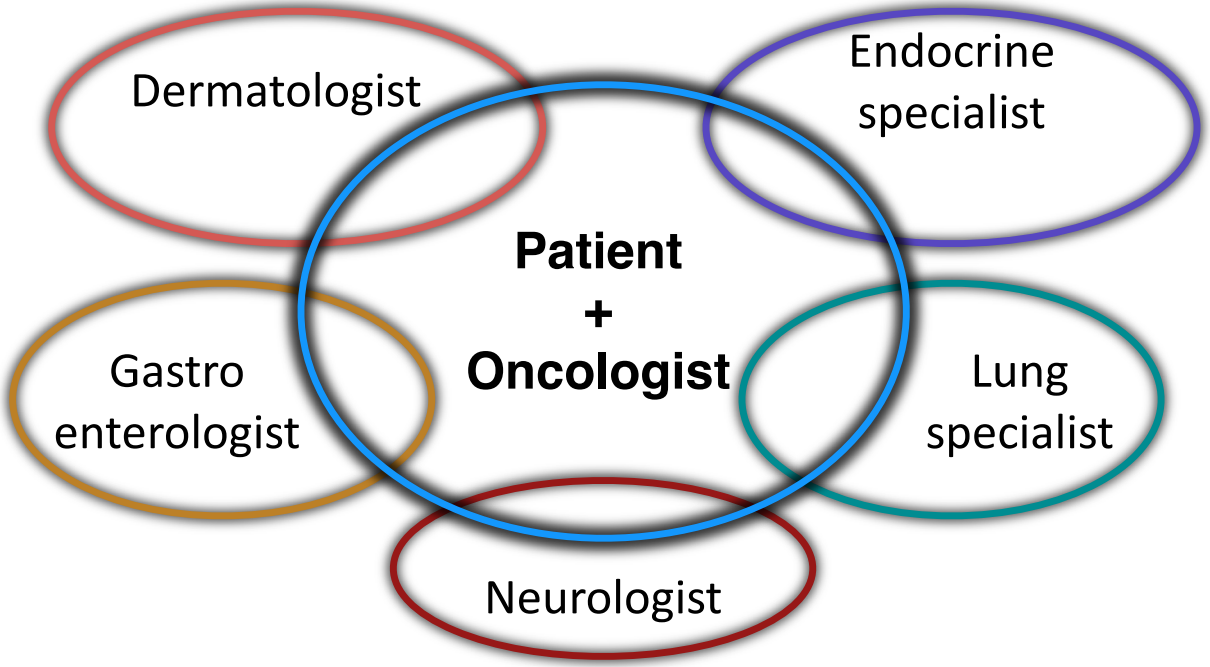
- Pulmonary embolism
- Pneumonitis
- Viral cardiomyopathy

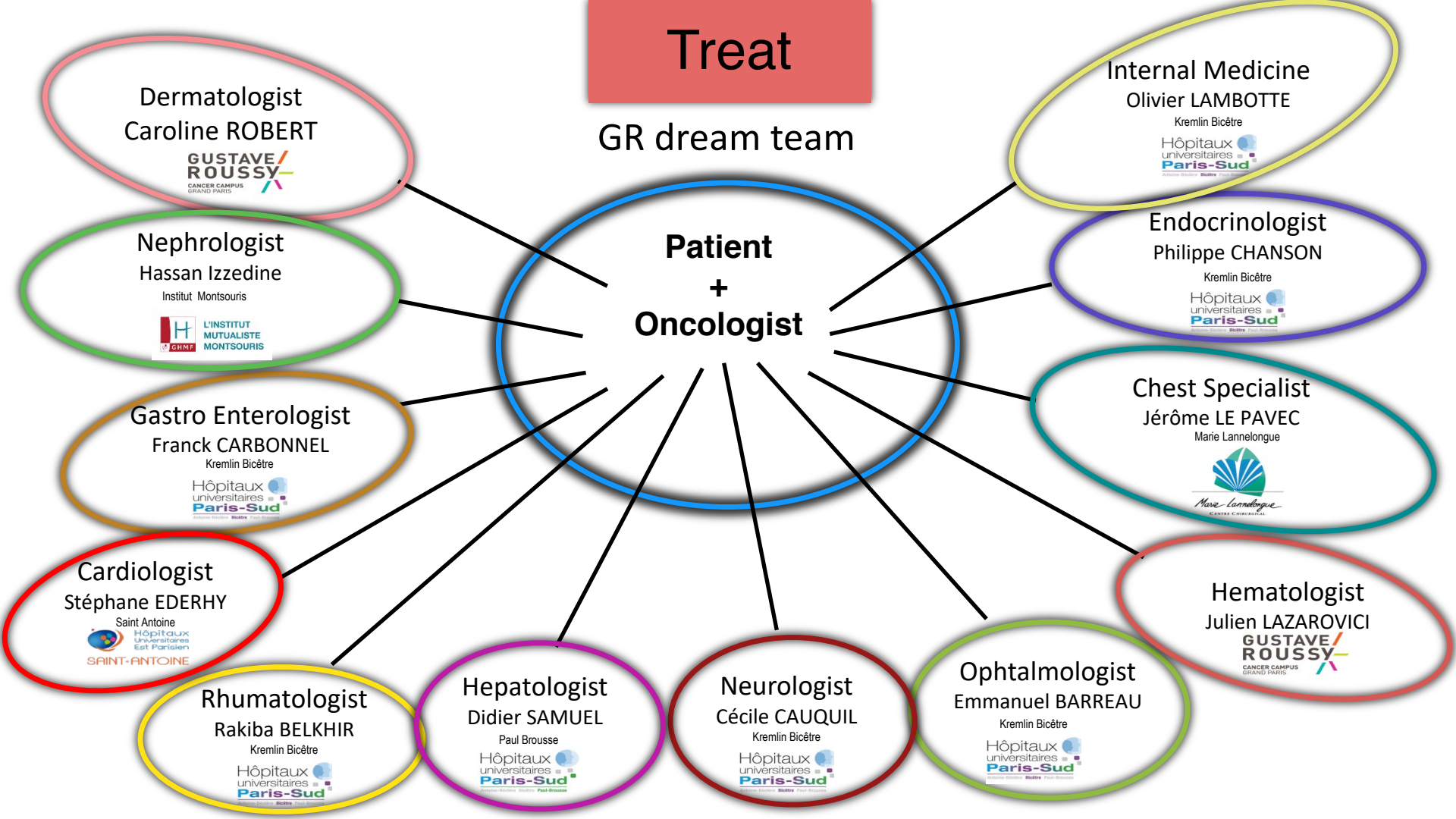
=> CT scan

# Treat

## Define your dream team

a multidisciplinary approach




Treat
GR dream team
Patient
+
Oncologist
Dermatologist
Caroline ROBERT
GUSTAVE ROUSSY
CANCER CAMPUS GRAND PARIS
Nephrologist
Hassan Izzedine
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# irAEs management tools

**Education**
**Pharmacovigilance**
New toxicities
Database

**Contraindication to ICI?**

**Immuno TOX board**

**Management ?**

**Re-challenge ?**

**RCP.iTOX@gustaveroussy.fr**


Gustave Roussy APP
French language

**Follow the latest publications on toxicities of immunotherapies**

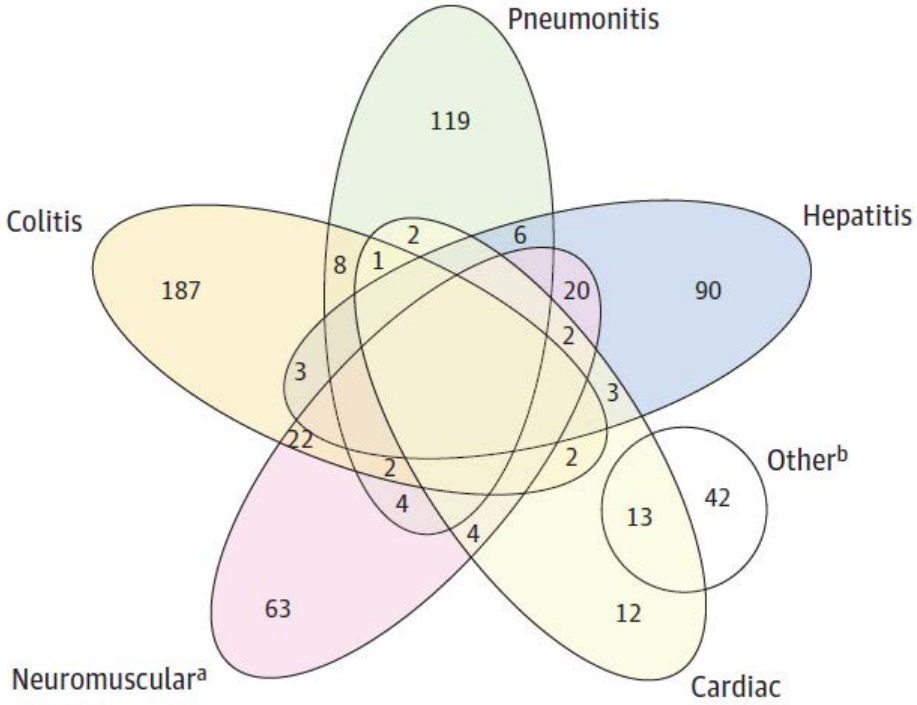
**@iTOXreport**

# Monitor

- **Close monitoring of treatment response**
- **Risk of relapse**
- **The occurrence of dysimmunitary toxicity**

  **does not prevent the occurrence of other toxicities**
- **Complications related to immunosuppression**

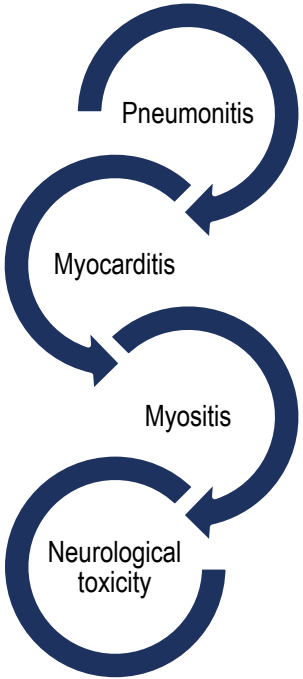
# Overlap of co-occurring fatal irAEs including colitis, pneumonitis, hepatitis,




Wang et al. JAMA Oncology 2018

# LIFE THREATENING TOXICITIES

## Key reflex to keep in mind …




- When you suspect a pneumonitis, look for a myocarditis
- Heart is a muscle like any other :

  if you suspect a myositis, look for a myocarditis

  if you suspect a myocarditis, look for a myositis
- If you have neurological symptoms, look for muscle abnormalities
- If you have muscular or heart abnormalities, look for neurological symptoms

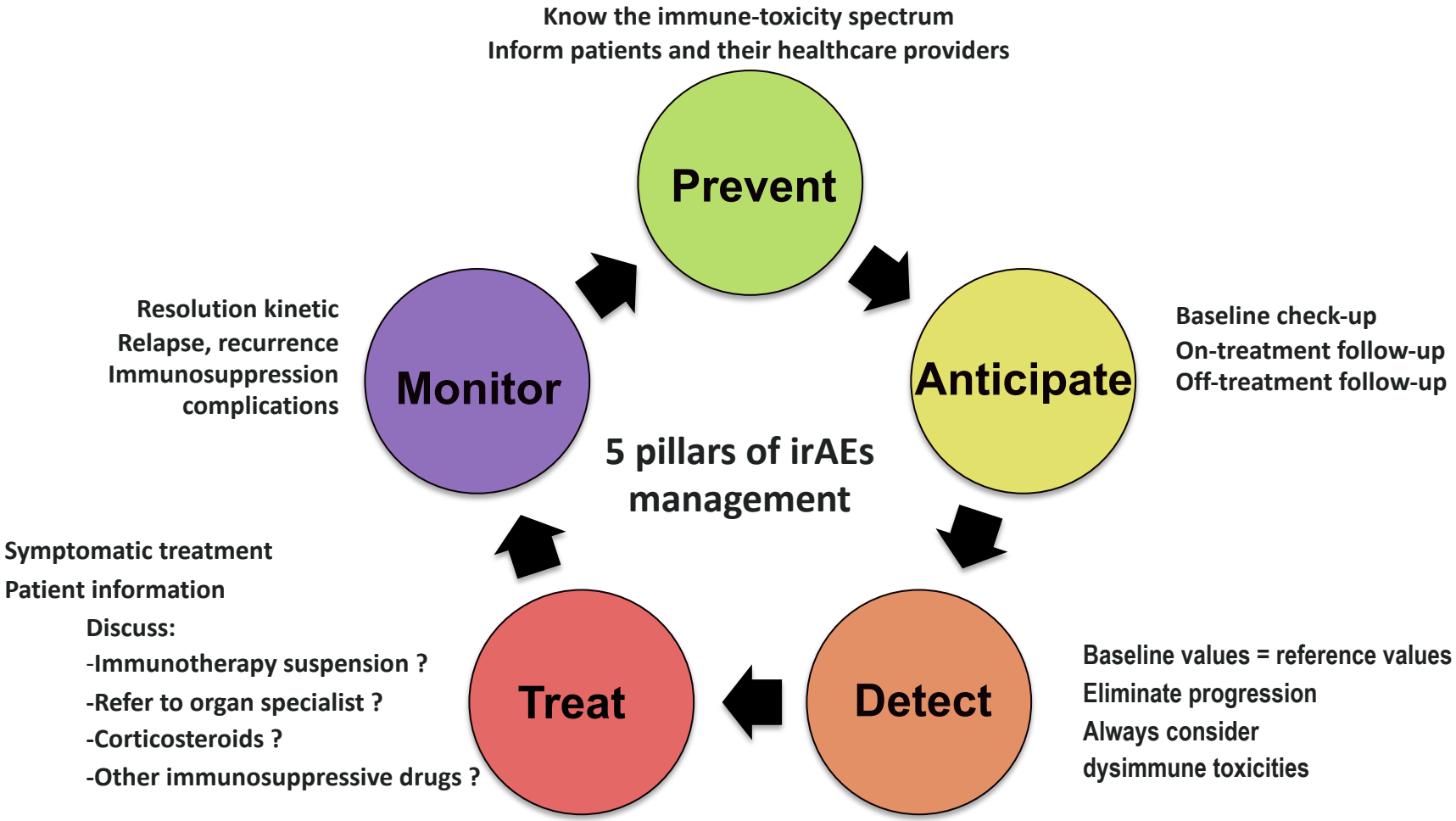
- **In any unusual situation** :
  - ✓ check cortisol and think **hydrocotisone**
  - ✓ check heart and muscle

# Monitor

- Close monitoring of treatment response
- Risk of relapse
- The occurrence of dysimmunitary toxicity

  does not prevent the occurrence of other toxicities
- Complications related to immunosuppression

**If Relapse or corticosteroid resistance :**
**ALWAYS look AGAIN**
**for differential diagnostics ++++++**



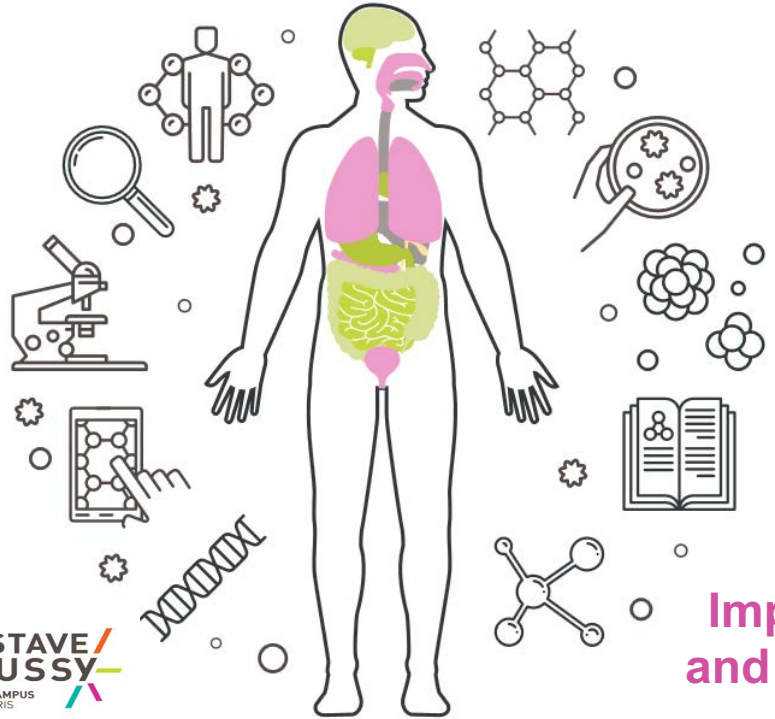

Champiat et al. (2016). *Annals of Oncology*

# iTOX 2020

*A symposium dedicated to immunotherapies' toxicities*

**14-15 May 2020, Paris, France**

**Medical oncologist**
**Hematologist**
**Organ's specialists**
**Pharmacists**
**Researchers**



**Share experience**

**Favor collaborations**

**Improve understanding and management of irAEs**

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CANCER CAMPUS
GRAND PARIS

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Christophe Massard
Aurélien Marabelle
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