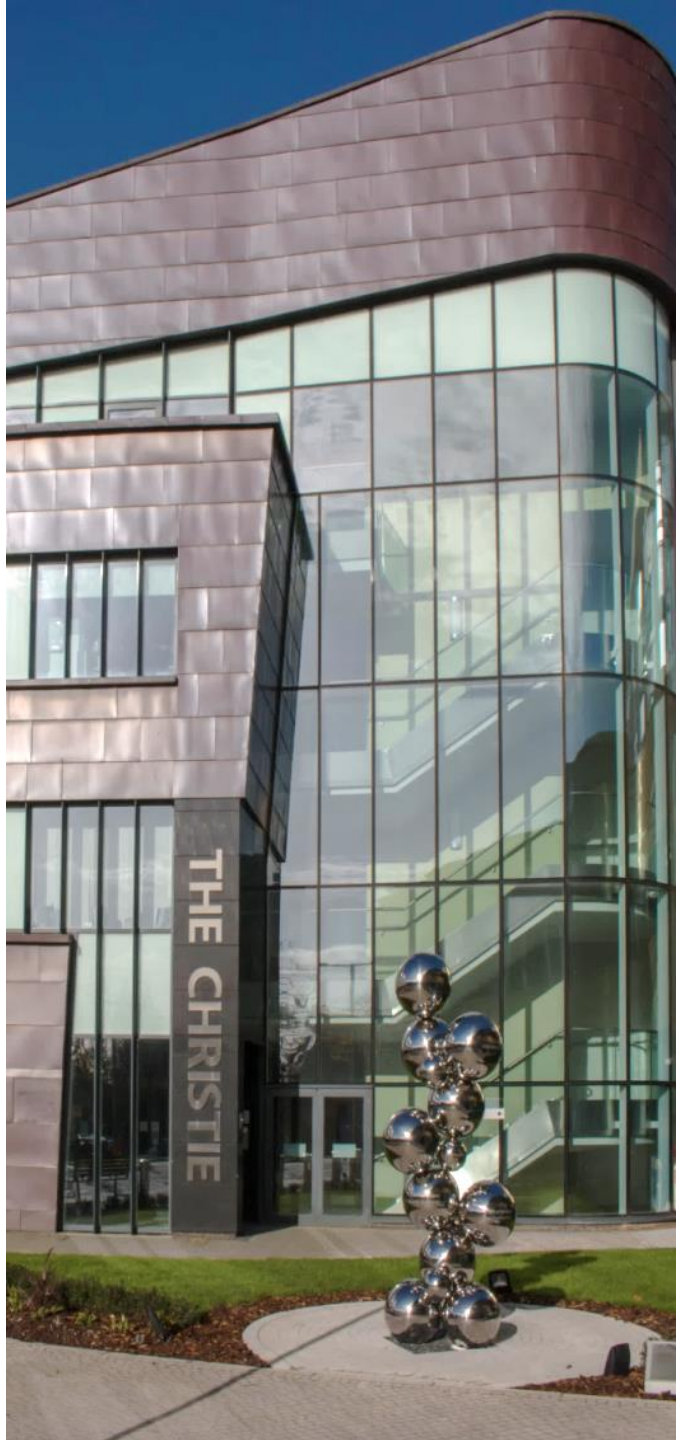


# Emergency management of high risk neutropenic sepsis

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# Overview

- Emergency approach to high risk neutropenic sepsis (MASCC < 21)
- Current guidelines
- Innovations to meet guidelines

# “Surviving Sepsis Campaign”

*Intensive Care Med (2018) 44:925–928*
https://doi.org/10.1007/s00134-018-5085-0

SPECIAL EDITORIAL

## The Surviving Sepsis Campaign Bundle: 2018 update

Mitchell M. Levy[1*], Laura E. Evans[2] and Andrew Rhodes[3]

# Surviving sepsis – 1st Hour

- Measure lactate.  (Re-measure if initial lactate >2mmol/L)
- Obtain blood cultures prior to administration of antibiotics
    - Paired cultures in those with indwelling line
- Administer broad spectrum antibiotics
    - Assume neutropenia in those post SACT
- Begin rapid administration of 30ml/kg crystalloid for hypotension or lactate >4mmol/L
- Commence vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥65mm Hg

# Initial history and examination

- Detailed clinical history
  - Infective symptoms
  - Type of SACT, **Cycle** of treatment, Use of corticosteroids, Use of antimicrobial prophylaxis
- Thorough clinical examination
  - Examine exit sites of indwelling catheters
  - Respiratory, GI, Oropharynx, Skin, Peri-anal regions, CNS for signs of infection
- Note any previous positive microbiology results

# Initial investigations

- Urgent bloods to assess marrow function, liver and renal function
- Clotting screen
- C Reactive Protein and Lactate
- Blood cultures (paired cultures if indwelling line in situ)
- Chest x-ray
- Urine culture
- Stool culture and sputum culture (if symptomatic)

- If no positive cultures and on-going fevers at 72 hours consider HRCT Thorax, BAL or CT abdomen

# Initial antibiotics

- Deliver broad spectrum IV antibiotics within 1 hour
- Be guided by local bacterial isolate and resistance patterns

    Aminoglycosides will be required in areas with resistant gram negative organisms
- Avoid aminoglycosides within 7 days of patients receiving platinum-based chemotherapy
- Consider glycopeptide in patients with high clinical suspicion for line infection

# Improving time to first dose IVABx

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NHS Manchester University NHS Foundation Trust

Support Care Cancer (2016) 24:5001–5005
DOI 10.1007/s00520-016-3362-4

ORIGINAL ARTICLE

## A nurse-led protocol improves the time to first dose intravenous antibiotics in septic patients post chemotherapy

Graeme Mattison[1] · Matthew Bilney[1] · Phil Haji-Michael[1] · Tim Cooksley[1]

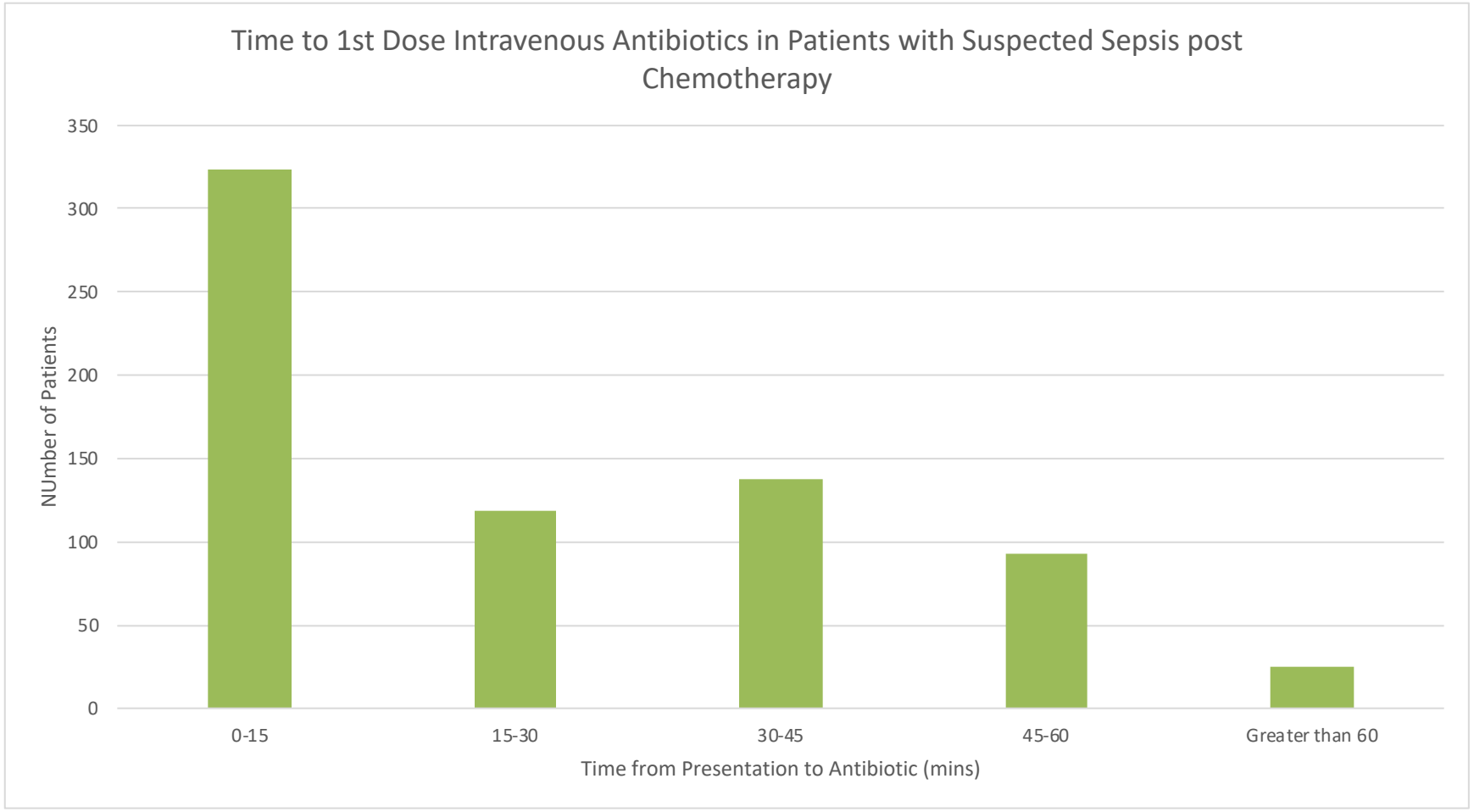
Received: 12 April 2016 / Accepted: 18 July 2016 / Published online: 25 July 2016


**Abstract**
*Purpose* Neutropenic sepsis is a time-dependent emergency with early interventions shown to improve outcomes. Broad spectrum intravenous antibiotic administration is the initial therapy in patients with suspected neutropenic sepsis. Compliance with early antibiotic administration in febrile neutropenia patients is poor. Innovations have been trialled to improve the time to first dose intravenous antibiotics in patients with suspected neutropenic sepsis. Consideration of extending first dose intravenous antibiotic prescribing to trained

*Conclusion* Nurse-led protocols are an effective, safe, and sustainable method for achieving early antibiotic administration in patients with suspected febrile neutropenia. This is a key component of ensuring improved outcomes for this cohort of patients.

**Keywords** Neutropenia · Sepsis · Time to antibiotics · Nurse-led · Chemotherapy

# Time to antibiotics



# Role of rescue G-CSF

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update

Thomas J. Smith, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, Baltimore, MD; Kari Bohlke, American Society of Clinical Oncology, Alexandria; Scott

*Thomas J. Smith, Kari Bohlke, Gary H. Lyman, Kenneth R. Carson, Jeffrey Crawford, Scott J. Cross, John M. Goldberg, James L. Khatcheressian, Natasha B. Leighl, Cheryl L. Perkins, George Somlo, James L. Wade, Antoinette J. Wozniak, and James O. Armitage*

- No role for routine rescue G-CSF
- G-CSF should have been administered prophylactically if the risk of FN is >20%
- Consider administering in high risk neutropenic sepsis patients who may respond to G-CSF
- Case reports of ARDS relating to G-CSF induced neutrophil recovery

# Steroids in high risk sepsis


## Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhandari, Y. Arabi, R. Bellomo, L. Billot, M. Correa, P. Glass, M. Harward, C. Joyce, Q. Li, C. McArthur, A. Perner, A. Rhodes, K. Thompson, S. Webb, and J. Myburgh, for the ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group*

- ADRENAL Trial (RCT of 3800 patients with septic shock given 200mg IV hydrocortisone OD vs placebo)
- Hydrocortisone did not result in lower 90 day mortality

# Steroids in high risk sepsis

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

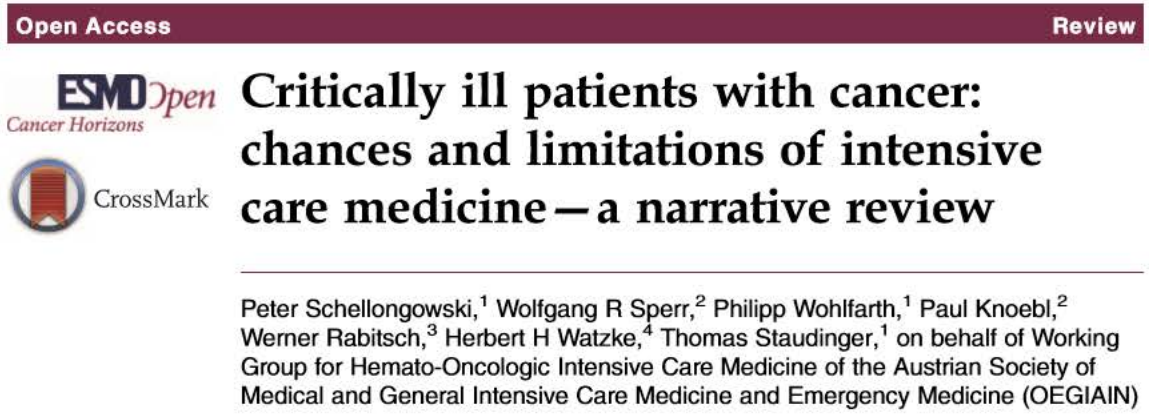
D. Annane, A. Renault, C. Brun-Buisson, B. Megarbane, J.-P. Quenot, S. Siami, A. Cariou, X. Forceville, C. Schwebel, C. Martin, J.-F. Timsit, B. Misset, M. Ali Benali, G. Colin, B. Souweine, K. Asehnoune, E. Mercier, L. Chimot, C. Charpentier, B. François, T. Boulain, F. Petitpas, J.-M. Constantin, G. Dhonneur, F. Baudin, A. Combes, J. Bohé, J.-F. Loriferne, R. Amathieu, F. Cook, M. Slama, O. Leroy, G. Capellier, A. Dargent, T. Hissem, V. Maxime, and E. Bellissant, for the CRICS-TRIGGERSEP Network*

- APROCHSS Trial (Randomised 2x2 study of 1241 septic shock patients given hydrocortisone plus fludrocortisone vs placebo)
- 90 day mortality was lower in patients who received hydrocortisone/fludrocortisone.

# Steroids in high risk neutropenic sepsis

- Corticosteroids may reduce the risk of death by a small amount and increase the risk of neuromuscular weakness by a small amount in high risk sepsis
- Patients with high risk neutropenic sepsis more likely to have had previous steroid exposure and adrenal dependence which may swing balance towards corticosteroids

# Escalation of care in neutropenic sepsis



Open Access Review

ESMO Open Cancer Horizons

CrossMark

## Critically ill patients with cancer: chances and limitations of intensive care medicine—a narrative review

Peter Schellongowski,[1] Wolfgang R Sperr,[2] Philipp Wohlfarth,[1] Paul Knoebl,[2] Werner Rabitsch,[3] Herbert H Watzke,[4] Thomas Staudinger,[1] on behalf of Working Group for Hemato-Oncologic Intensive Care Medicine of the Austrian Society of Medical and General Intensive Care Medicine and Emergency Medicine (OEGIAIN)

- High risk neutropenic sepsis patients can deteriorate rapidly
- Require close monitoring in emergency setting
- Need early decisions regarding ceilings of care, whether organ support in intensive care is appropriate and DNAR documentation

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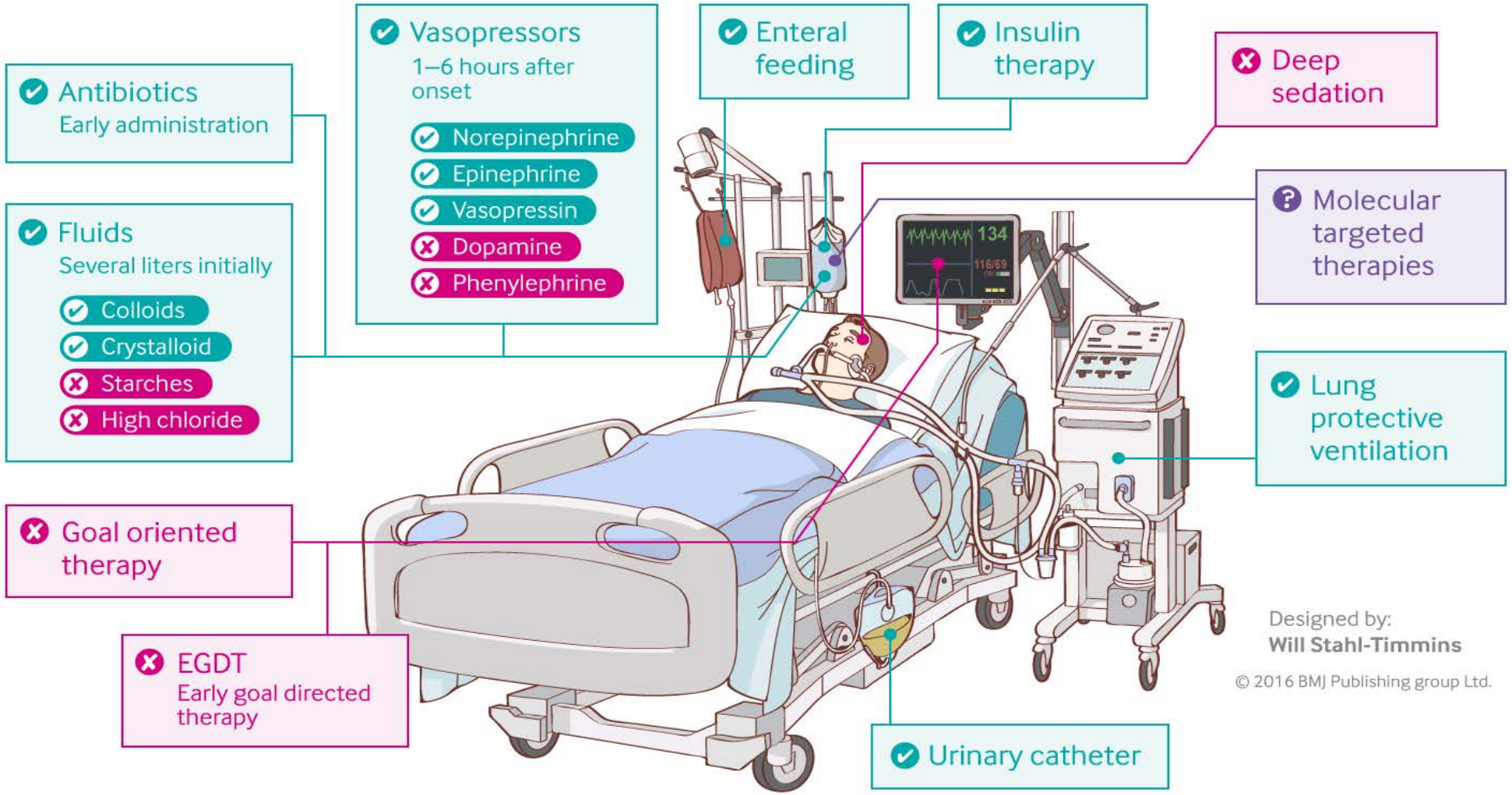
# Treating sepsis: the latest evidence



# Case History

- 62 year old lady with metastatic breast cancer
- Cycle 1 Day 4 Capecitabine
- Presents with fever, oral pain, diarrhoea and fatigue
- No other significant medical history

- On examination – unwell, pyrexial and dehydrated
- BP = 100/50mmHg, Pulse =110bpm
- Grade 3 oral mucositis
- Rest of systemic examination unremarkable

# Initial investigations and treatment

- Grade 4 neutropenia (ANC = 0.4 x $10^9$/L)
- AKI and Lactate = 3.2
- Treated with IV Tazobactam/Piperacillin
- IV fluid resuscitation
- IV anti-emetics/Mouthwashes/TPN/Pressure area care
- IV hydrocortisone
- Continued rapid deterioration – transferred to ICU for vasopressors

# DPD Deficiency/ Uridine Triacetate

Cancer

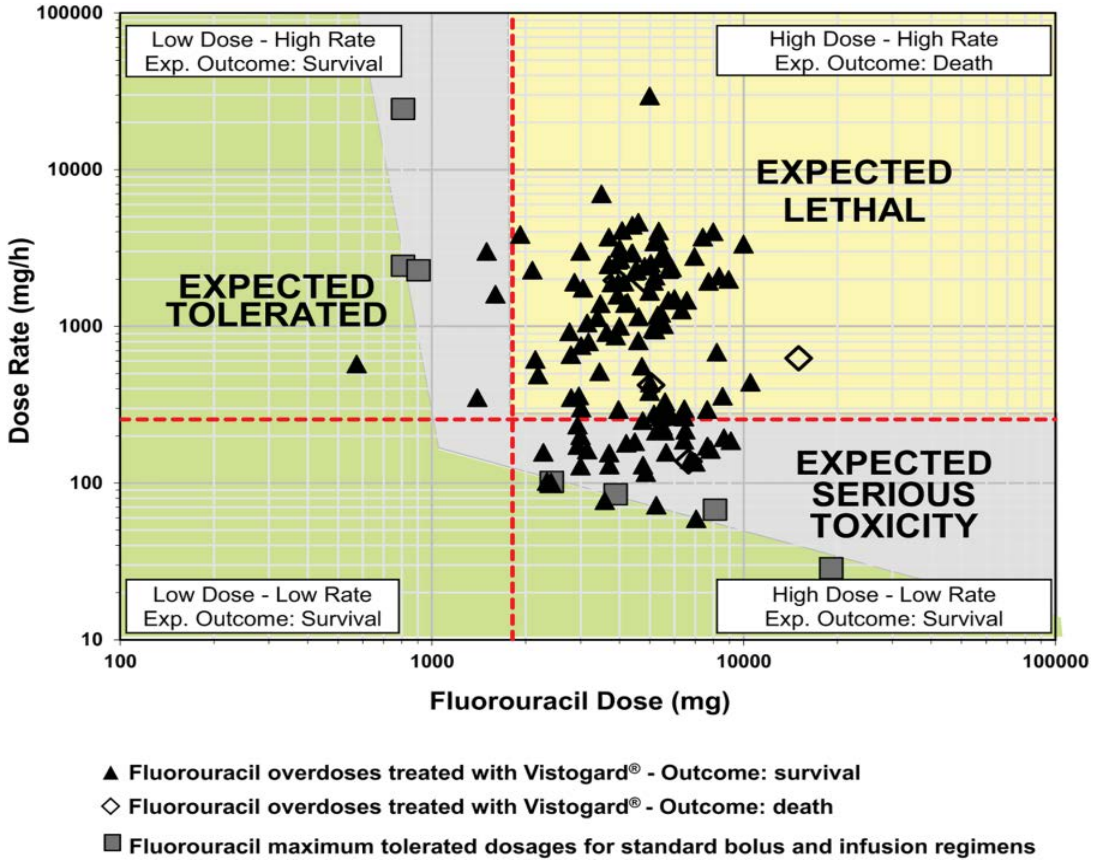
Original Article | Open Access

## Emergency use of uridine triacetate for the prevention and treatment of life-threatening 5-fluorouracil and capecitabine toxicity

Wen Wee Ma MD, Muhammad Wasif Saif MD, Bassel F. El-Rayes MD ... See all authors

First published: 13 September 2016 | https://doi.org/10.1002/cncr.30321 | Cited by: 12

# Uridine Triacetate



# Case History : Next generation of high risk febrile neutropenia

- 38 year old lady with metastatic colorectal carcinoma
- Completed 2 cycles of Nivolumab
- Presented with fever and myalgia
- No focal symptoms
- No symptoms of other immune-mediated toxicity

- Febrile, Tachypnoeic, Tachycardic

- Neuts = 0.2 (MASCC = 24)

# Management and progress

- Treated with
  - Intravenous antibiotics
  - G-CSF
  - Physiological steroids
  - Supportive treatment

- Good clinical progress
- Cultures negative
- Neutrophils recovered

Case Report

# Refractory Neutropenia Secondary to Dual Immune Checkpoint Inhibitors That Required Second-Line Immunosuppression

*Nicholas Meti, Tina Petrogiannis-Haliotis, and Khashayar Esfahani*

Anti-Cancer Drugs. 29(8):817–819, SEP 2018
DOI: 10.1097/CAD.0000000000000661, PMID: 29889673
Issn Print: 0959-4973
Publication Date: 2018/09/01

# A case of severe Pembrolizumab-induced neutropenia

Ariane Barbacki;Peter Maliha;Marie Hudson;David Small;

+ Author Information

# Conclusions

- High risk neutropenic sepsis has significant mortality
- Requires impeccable initial clinical work-up
- Early IV antibiotics and source control is main goal of treatment
- Innovative practice is required to achieve early IV antibiotics
- Excellent supportive treatment
- Close clinical monitoring
- Immune-mediated neutropenic sepsis on its way
- Early decisions regarding escalation of care