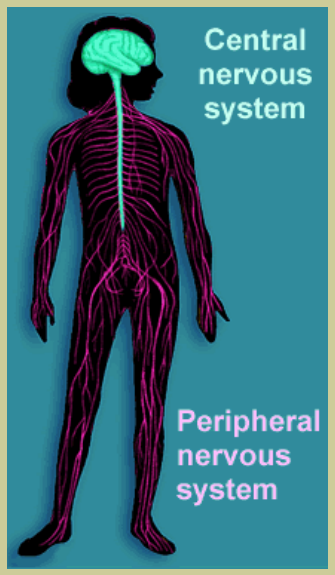

Απαρτιωμένη Διδασκαλία στην Ογκολογία

Νευρολογικά προβλήματα ασθενών με καρκίνο

Ανδρέας Α. Αργυρίου, MD, PhD

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Γενικού Νοσοκομείου Πατρών "Ο Άγιος Ανδρέας"
Διδάκτωρ Πανεπιστημίου Πατρών

Νευρικό σύστημα και καρκίνος

- Απευθείας προσβολή του ΝΣ από το καρκίνο
  - **Εγκεφαλικοί όγκοι και μεταστάσεις**
  - **Καρκινοματώδης μηνιγγίτιδες και εγκεφαλίτιδες**
  - **Παραναεοπλασματικά σύνδρομα**
- Προσβολή ΚΝΣ από τη χορήγηση ΧΜΘ
  - **Εγκεφαλοπάθεια (**σύνδρομο οπίσθιας αναστρέψιμης εγκεφαλοπάθειας [*Posterior Reversible Encephalopathy Syndrome*]
  - **Νοητική έκπτωση**
- Προσβολή ΠΝΣ από τη χορήγηση ΧΜΘ
  - **Περιφερική τοξική πολυνευροπάθεια**

Απευθείας προσβολή του ΝΣ από το καρκίνο

Σχετική συχνότητα εμφάνισης των όγκων του ΝΣ στους ενήλικες

όγκοι ΚΝΣ = **8 -10%** των πρωτοπαθών όγκων
= **1,5-2%** των θανάτων από καρκίνο.

Επίπτωση = πρωτοπαθείς **15,3/100.000** κατ.
(UK data) δευτεροπαθείς **14,3/100.000** κατ.

- Γλοιώματα 70%
- Μηνιγγιώματα 10%
- Αδενώματα Υπόφυσης 10%
- Ακουστικά Νευρινώματα 5%
- Άλλοι όγκοι 5%

Πρωτοπαθείς 80% Μεταστατικοί 20%

Τύποι καρκίνου

Brain mets common

- Lung (50%)
- Breast (15-20%)
- Unknown Primary (10%)
- Melanoma (10%)

Brain mets rare

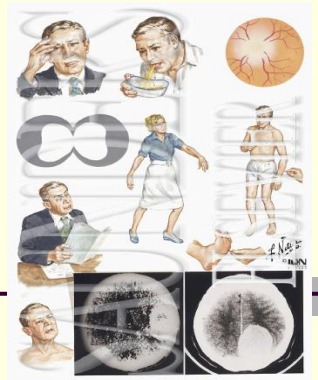
- Esophagus
- Oropharynx
- Non-melanoma skin cancer
- Prostate

TABLE 1. Primary Tumor Type in 729 Patients with Brain Metastases

Primary Type	No. Total (%)	No. Single (%)	No. Multiple (%)
NSCLC	178 (24)	89 (50)	89 (50)
Breast	121 (17)	59 (49)	62 (51)
SCLC	110 (15)	48 (43)	62 (56)
Melanoma	80 (11)	39 (49)	41 (51)
Renal cell	45 (6)	25 (56)	20 (44)
Gastrointestinal	45 (6)	30 (67)	14 (33)
Uterine/vulvar	38 (5)	20 (53)	18 (47)
Unknown	33 (5)	23 (70)	10 (30)
Ovarian	14 (2)	8 (57)	6 (43)
Bladder	14 (2)	9 (64)	5 (36)
Prostate	11 (2)	9 (82)	2 (18)
Testicular	11 (2)	6 (55)	5 (45)
Miscellaneous	29 (4)	19 (65)	345 (47)
Total	729/100	384 (53)	345 (47)

NSLC = nonsmall cell lung carcinoma, SCLC = small cell lung cancer.

Εγκεφαλικοί όγκοι και μεταστάσεις



Τα συμπτώματα εξαρτώνται από τη θέση, το ρυθμό αύξησης και την ιστολογία του πρωτοπαθούς όγκου και τον όγκο του οιδήματος.

Κλινικά εκδηλώνονται

είτε **οξέως** (επιλήπτ. κρίσεις, αιφνίδια σύγχυση)

είτε **βαθμιαία και «ύπουλα»**

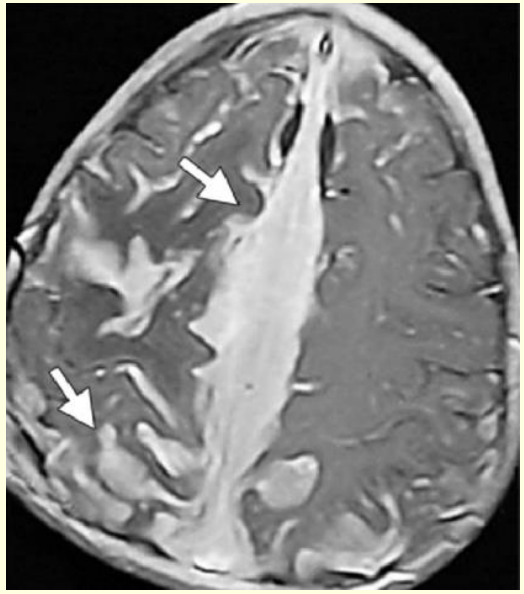
(βραδεία μεταβολή στις κινητικο-αισθητικές λειτουργίες, στην προσωπικότητα ή τη γνωσία)

Τα συμπτώματα διακρίνονται σε

1. **Γενικευμένα συμπτώματα (αύξηση ενδ/κράνιας Π)**
2. **Εστιακά συμπτώματα (ημιπάρεση, διατ. Όρασης, Επιληψία**

Καρκινωματώδεις μηνιγγίτιδες / εγκεφαλίτιδες

- Αφορά περίπου 5% των ασθενών με καρκίνο
- Κυρίως μετά από breast cancer, lung cancer, melanoma, GI malignancy
- Κλινική εμφάνιση: συμπτωματολογία αύξησης ενδοκράνιας πίεσης, σύγχυση, επιληπτικές κρίσεις
- Τυπικά MRI ευρήματα: διάχυτη λεπτομηνιγγική διήθηση.
- Τυπικά CSF ευρήματα: Υψηλή πίεση, χαμηλή γλυκόζη, αυξημένο λεύκωμα, λεμφοκυτταρική πλειοκυττάρωση, αρνητικές καλλιέργειες και χρώσεις, κυτταρολογική με καρκινικά κύτταρα



Παρανεοπλασματικά σύνδρομα

- Αφορούν< 1% των ασθενών με καρκίνο
- Προηγούνται της διάγνωσης του καρκίνου σε ποσοστό 60%
- Ανευρίσκονται ειδικά αντινευρωνικά αντισώματα
- Πλέον συχνά σύνδρομα
  - Paraneoplastic cerebellar degeneration (PCD)
  - Paraneoplastic encephalomyelitis / sensory neuronopathy (PEM/PSN)
  - Paraneoplastic opsoclonus myoclonus (POM)
  - Lambert-Eaton myasthenic syndrome (LEMS)
  - Axonal peripheral neuropathy

Προσβολή ΝΣ από τη χημειοθεραπεία

Καρκίνος και ΧΜΘ

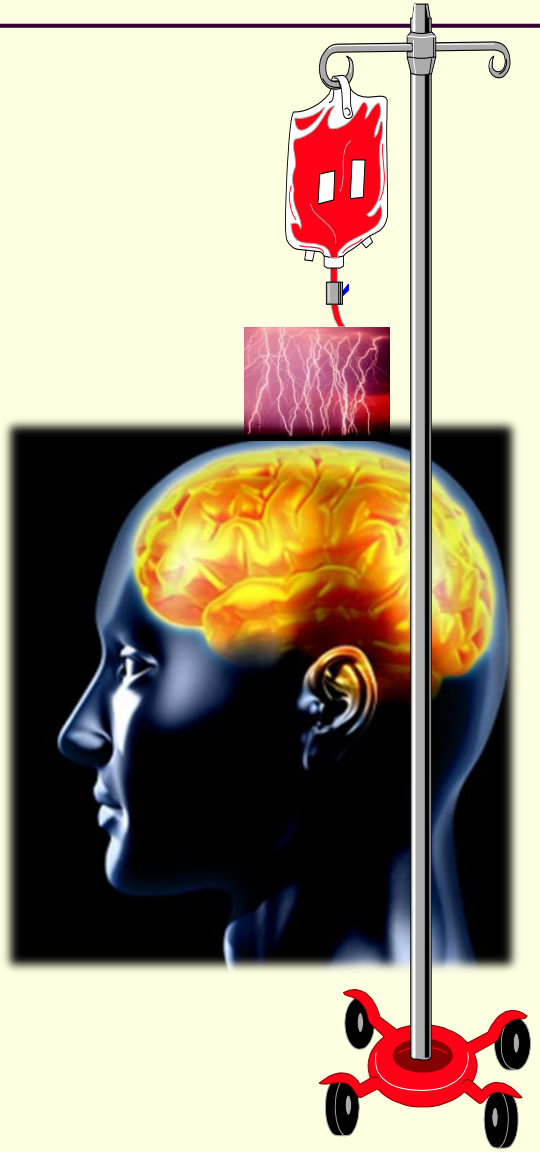
- 10.000.000 επιβιώσαντες από καρκίνο στις ΗΠΑ
- Αντιστοίχως μεγάλοι αριθμοί στην Ευρώπη
- Οι επιβιώσαντες από Ca μαστού αποτελούν την πλειοψηφία (22% ή 1.900.000).
- *"fastest growing club no one ever wanted to belong to"*

Γιατί μας ενδιαφέρει??

- Συχνή και σε πολλές περιπτώσεις δοσοπεριοριστική τοξικότητα
- Αρνητική επιρροή στην ποιότητα ζωής και προσδόκιμο
- Απρόβλεπτη και ποικίλη έκβαση
- Συχνά η δ.δ. από μεταστατική νόσο, λοιμώξεις, παρανεοπλασματική νόσο, άλλες νευροπάθειες είναι δύσκολη
- Αντικρουόμενα δεδομένα για θεραπεία ή πρόληψη με νευροπροστατευτικές ουσίες

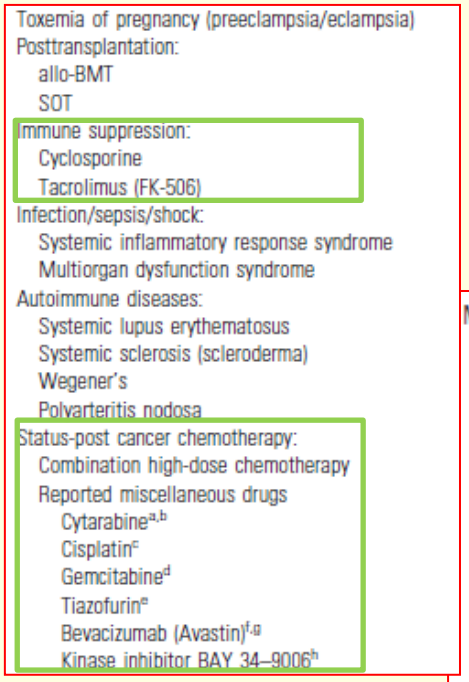
Η γνώση των πιο συχνών συνδρόμων που αφορούν την τοξική δράση της ΧΜΘ τόσο στο ΚΝΣ όσο και στο ΠΝΣ είναι ΑΠΑΡΑΙΤΗΤΗ

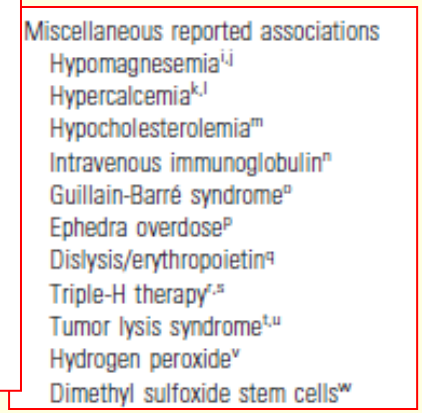
ΠΡΟΣΒΟΛΗ ΚΝΣ ΑΠΟ ΤΗ ΧΟΡΗΓΗΣΗ ΧΜΘ



Posterior Reversible Encephalopathy Syndrome-PRES

- PRES (σύνδρομο οπίσθιας αναστρέψιμης εγκεφαλοπάθειας: ένα σύνδρομο τοξικότητας του ΚΝΣ με χαρακτηριστικά νευροαπεικονιστικά ευρήματα
- Τυπικά ανευρίσκονται περιοχές με αμφοτερόπλευρο ημισφαιρικό ***αγγειογενές*** οίδημα στους βρεγματικούς και ινιακούς λοβούς.
- Οι μετωπιαίοι λοβοί και οι πρόσθιες κροταφο-ινιακές περιοχές προσβάλλονται επίσης συχνά

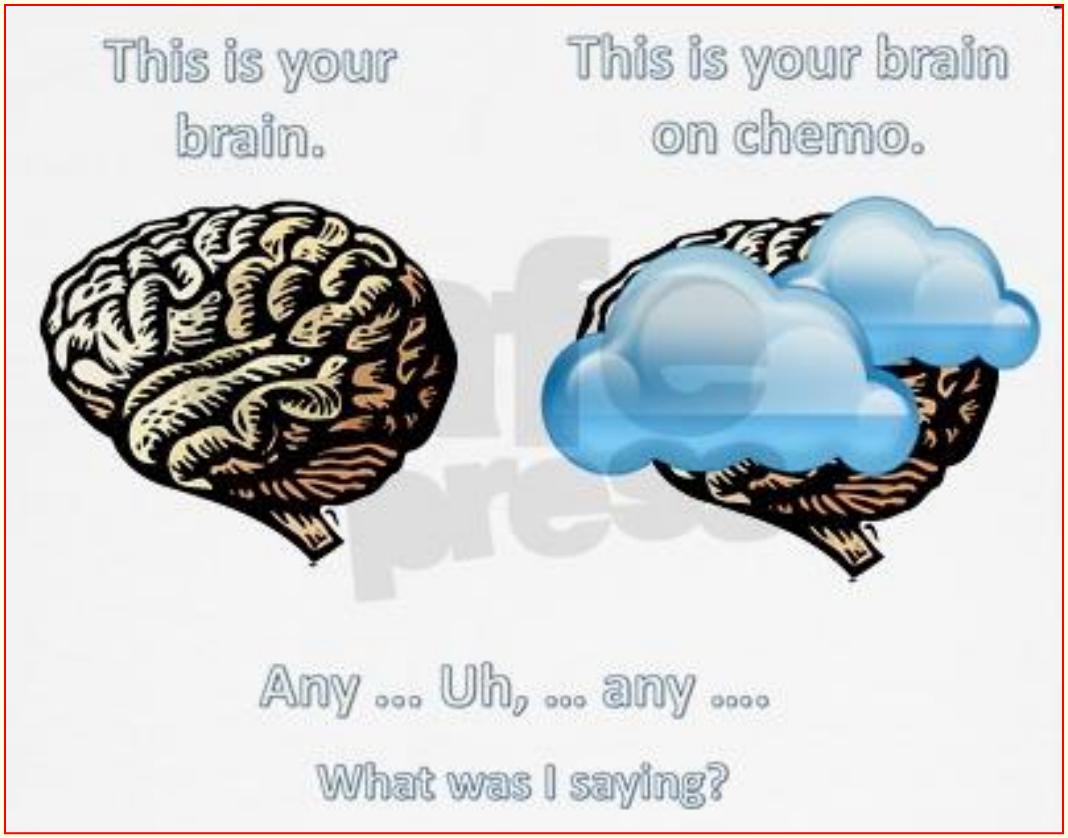




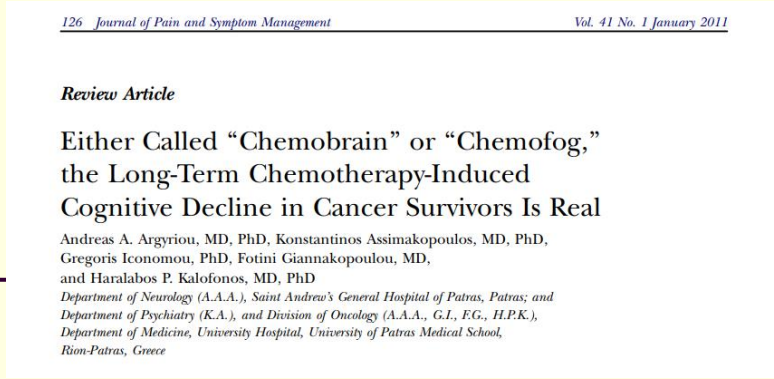
Κλινική εικόνα PRES

- Κεφαλαλγία, έμεση από αύξηση ενδοκράνιας πίεσης
- Διαταραχή επιπέδου συνείδησης από σύγχυση έως κωματώδης κατάσταση
- Διαταραχές όρασης με θάμβος, ημιανοψία ή φλοιώδη τύφλωση
- Επιληπτικοί σπασμοί – επαναλαμβανόμενα επεισόδια εστιακών ή γενικευμένων Ε κρίσεων
- Πυραμιδικά τενόντια αντανακλαστικά

Νοητική έκπτωση εξαιτίας της ΧΜΘ



Chemobrain



126 Journal of Pain and Symptom Management Vol. 41 No. 1 January 2011

Review Article

Either Called "Chemobrain" or "Chemofog," the Long-Term Chemotherapy-Induced Cognitive Decline in Cancer Survivors Is Real

Andreas A. Argyriou, MD, PhD, Konstantinos Assimakopoulos, MD, PhD, Gregoris Iconomou, PhD, Fotini Giannakopoulou, MD, and Haralabos P. Kalofonos, MD, PhD

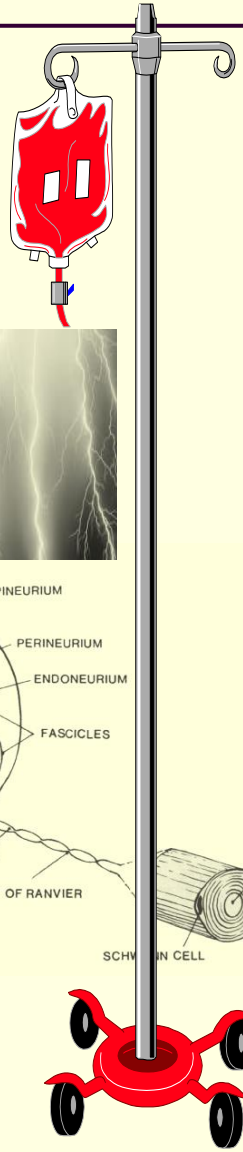
Department of Neurology (A.A.A.), Saint Andrew's General Hospital of Patras, Patras; and Department of Psychiatry (K.A.), and Division of Oncology (A.A.A., G.I., F.G., H.P.K.), Department of Medicine, University Hospital, University of Patras Medical School, Rion-Patras, Greece

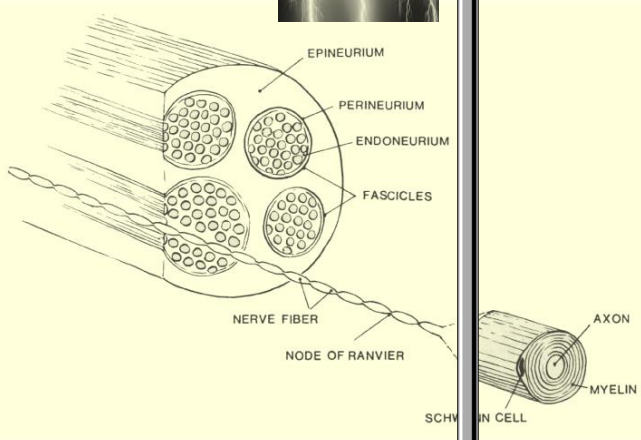
- Η δημοσιευμένη εμπειρία δείχνει:
  - **50-75%** των ασθενών αναφέρουν (self-report) κάποιου βαθμού νοητική έκπτωση
  - έκπτωση νοητικής ικανότητας, κυρίως μνήμη, προσοχή, εκτέλεση, κατά και μετά την ολοκλήρωση της ΧΜΘ
  - Μπορεί να είναι παροδική, ή να αφήσει μόνιμο έλλειμμα στη νόηση των ασθενών
  - Εμφανίζεται κυρίως μετά από ΧΜΘ για Ca μαστού, πνεύμονα, προστάτη, και ωοθηκών
- Χαμηλή συσχέτιση μεταξύ αναφερόμενων συμπτωμάτων από ασθενείς και αντικειμενική πιστοποίηση με ΝΨΔ

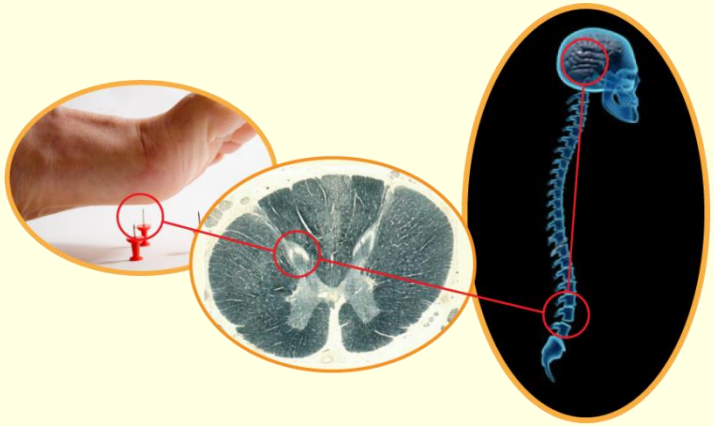
Συγχυτικοί (confounding) παράγοντες

- Ψυχολογικοί παράγοντες
  - Άγχος
  - Κατάθλιψη
- Κόπωση χωρίς αναιμία
- Ορμονοθεραπεία (μείωση οιστρογόνων στο ΚΝΣ)
  - Ταμοξιφένη
  - Αναστολείς αρωματάσης
  - Ανδρογόνα

ΠΡΟΣΒΟΛΗ ΠΝΣ ΑΠΟ ΤΗ ΧΟΡΗΓΗΣΗ ΧΜΘ

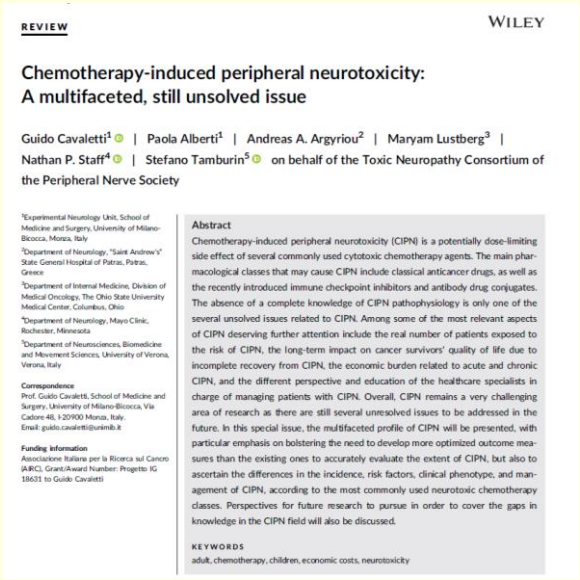






Το μέγεθος του προβλήματος…

- Η περιφερική νευροπάθεια εξαιτίας της χορήγησης ΧΜΘ αποτελεί έναν από τους κυριότερους ανασταλτικούς παράγοντες, που συχνά περιορίζουν τη χορήγηση της μέγιστης επιτρεπτής δόσης πολλών αποτελεσματικών στην καταπολέμηση του καρκίνου ΧΜΘ παραγόντων.
- Η ποιότητα ζωής των ασθενών υποβαθμίζεται σημαντικά
- Ο παθογενετικός μηχανισμός της περιφερικής νευροπάθειας δεν έχουν ακόμα καθορισθεί με ακρίβεια
- Τα κλινικά της χαρακτηριστικά ποικίλουν ανάλογα με το μηχανισμό δράσης των ΧΜΘ φαρμάκων και τη δομή του ΠΝΣ που προσβάλλουν
- Το φαινόμενο “coasting”



REVIEW

WILEY

Chemotherapy-induced peripheral neurotoxicity: A multifaceted, still unsolved issue

Guido Cavaletti[1] | Paola Alberti[1] | Andreas A. Argyriou[2] | Maryam Lustberg[3] | Nathan P. Staff[4] | Stefano Tamburin[5] on behalf of the Toxic Neuropathy Consortium of the Peripheral Nerve Society

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Abstract
Chemotherapy-induced peripheral neurotoxicity (CIPN) is a potentially dose-limiting side effect of several commonly used cytotoxic chemotherapy agents. The main pharmacological classes that may cause CIPN include classical anticancer drugs, as well as the recently introduced immune checkpoint inhibitors and antibody drug conjugates. The absence of a complete knowledge of CIPN pathophysiology is only one of the several unsolved issues related to CIPN. Among some of the most relevant aspects of CIPN deserving further attention include the real number of patients exposed to the risk of CIPN, the long-term impact on cancer survivors' quality of life due to incomplete recovery from CIPN, the economic burden related to acute and chronic CIPN, and the different perspective and education of the healthcare specialists in charge of managing patients with CIPN. Overall, CIPN remains a very challenging area of research as there are still several unresolved issues to be addressed in the future. In this special issue, the multifaceted profile of CIPN will be presented, with particular emphasis on bolstering the need to develop more optimized outcome measures than the existing ones to accurately evaluate the extent of CIPN, but also to ascertain the differences in the incidence, risk factors, clinical phenotype, and management of CIPN, according to the most commonly used neurotoxic chemotherapy classes. Perspectives for future research to pursue in order to cover the gaps in knowledge in the CIPN field will also be discussed.

KEYWORDS
adult, chemotherapy, children, economic costs, neurotoxicity

PAIN® 155 (2014) 2461–2470

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Comprehensive review

Incidence, prevalence, and predictors of chemotherapy-induced peripheral neuropathy: A systematic review and meta-analysis

Marta Seretny [a,*], Gillian L. Currie [b], Emily S. Sena [b], Sabrina Ramnarine [a], Robin Grant [c], Malcolm R. MacLeod [b], Leslie A. Colvin [c], Marie Fallon [a]

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ABSTRACT

Chemotherapy-induced peripheral neuropathy (CIPN) is a disabling pain condition resulting from chemotherapy for cancer. Severe acute CIPN may require chemotherapy dose reduction or cessation. There is no effective CIPN prevention strategy; treatment of established chronic CIPN is limited, and the prevalence of CIPN is not known. Here we used a systematic review to identify studies reporting the prevalence of CIPN. We searched Embase, Medline, CAB Abstracts, CINAHL, PubMed central, Cochrane Library, and Web of Knowledge for relevant references and used random-effects meta-regression to estimate overall prevalence. We assessed study quality using the CONSORT and STROBE guidelines, and we report findings according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidance. We provide a qualitative summary of factors reported to alter the risk of CIPN. We included 31 studies with data from 4179 patients in our analysis. CIPN prevalence was 68.1% (57.7–78.4) when measured in the first month after chemotherapy, 60.0% (36.4–81.6) at 3 months and 30.0% (6.4–53.5) at 6 months or more. Different chemotherapy drugs were associated with differences in CIPN prevalence, and there was some evidence of publication bias. Genetic risk factors were reported in 4 studies. Clinical risk factors, identified in 4 of 31 studies, included neuropathy at baseline, smoking, abnormal creatinine clearance, and specific sensory changes during chemotherapy. Although CIPN prevalence decreases with time, at 6 months 30% of patients continue to suffer from CIPN. Routine CIPN surveillance during post-chemotherapy follow-up is needed. A number of genetic and clinical risk factors were identified that require further study.

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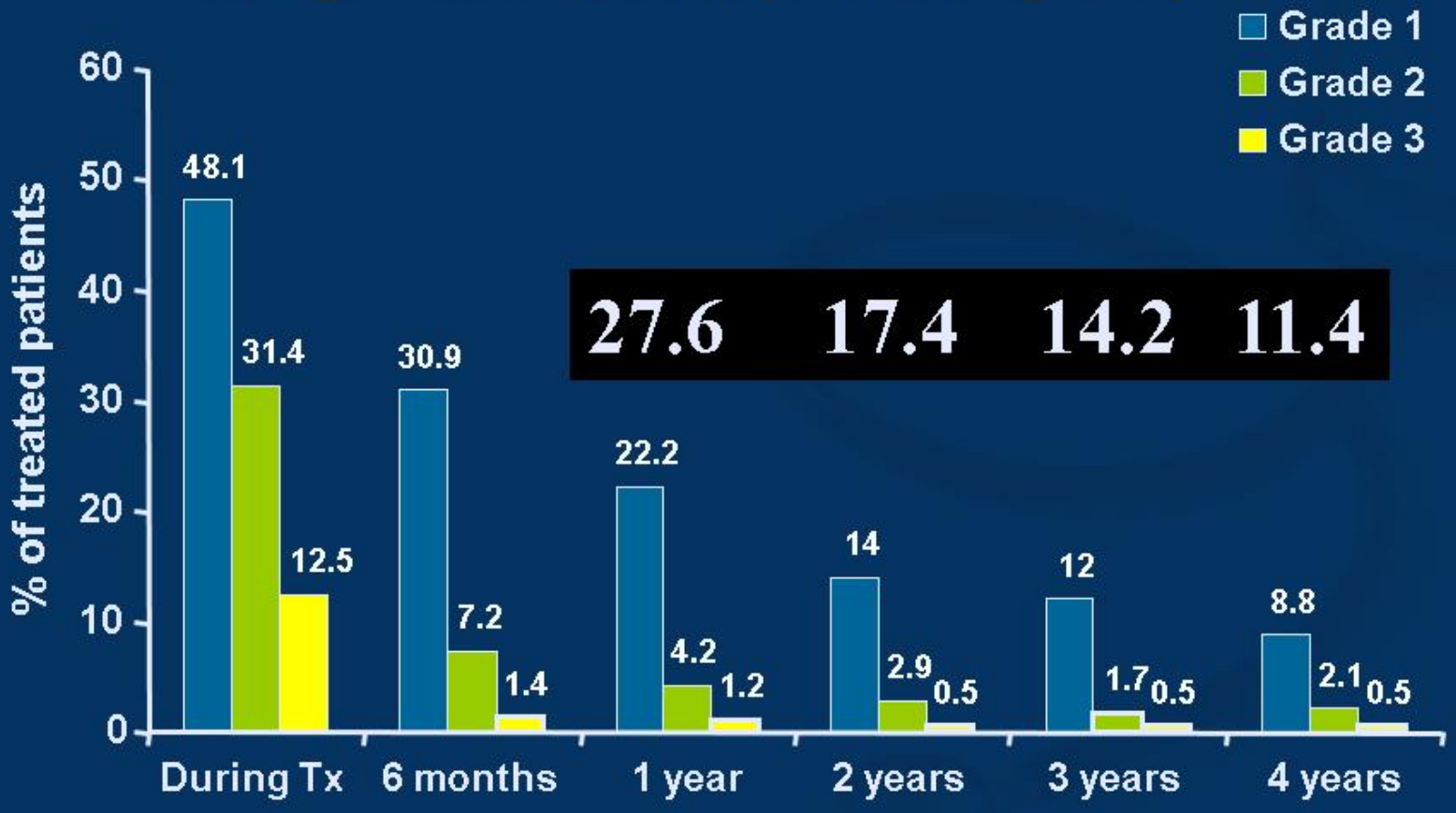
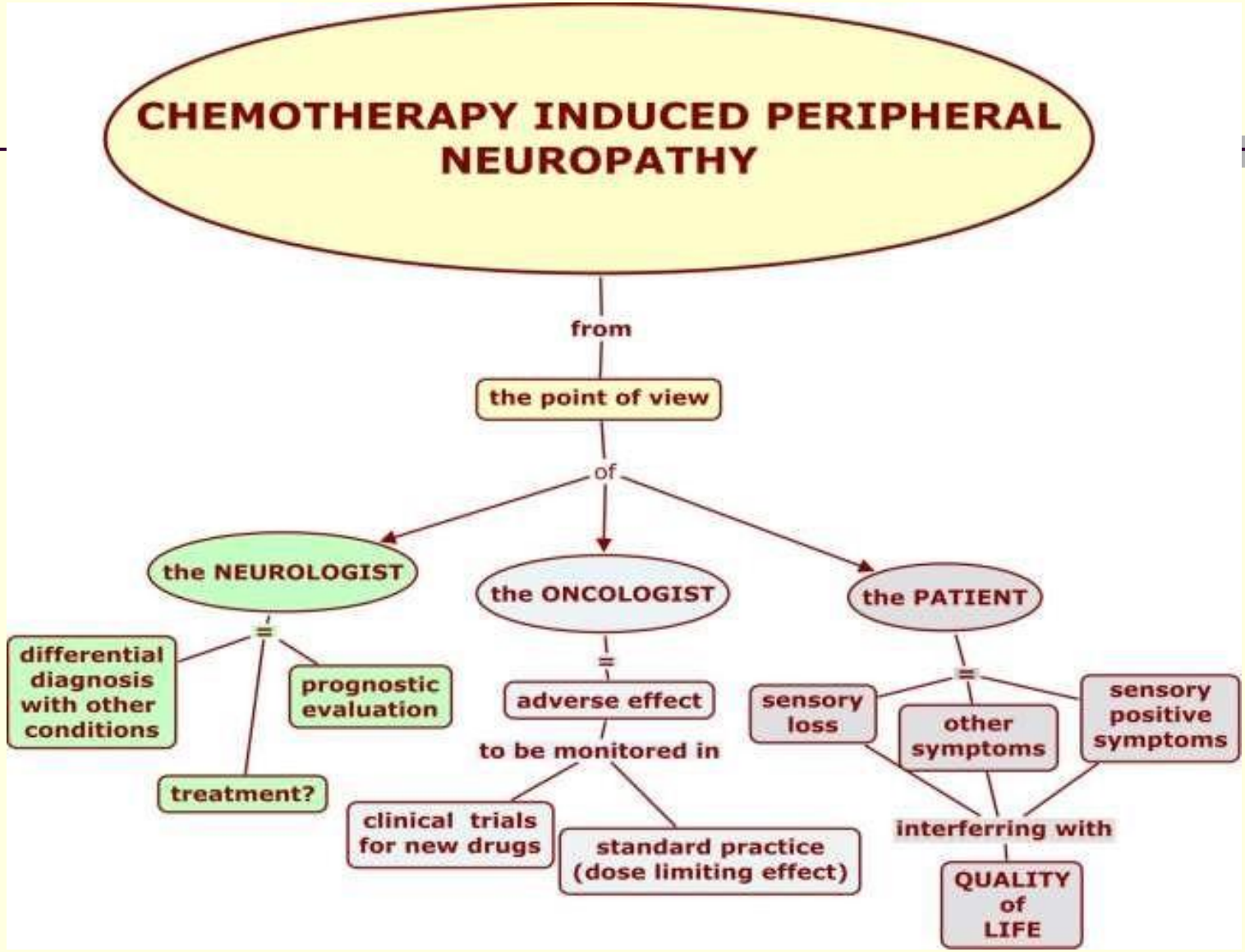
Peripheral Sensory Neuropathy




CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY
from
the point of view
of
the NEUROLOGIST
the ONCOLOGIST
the PATIENT
differential diagnosis with other conditions
prognostic evaluation
treatment?
adverse effect
to be monitored in
clinical trials for new drugs
standard practice (dose limiting effect)
sensory loss
other symptoms
sensory positive symptoms
interferring with
QUALITY of LIFE

Χημειοθεραπευτικοί παράγοντες που προκαλούν περιφερική νευροπάθεια

DRUG	prevalence	severity	relevance
VCR	+	++++	+
TAX	+++	++	++
DDP	+++	++	+++
OXALI	+++++	++++++	+++++

Κλινικές εκδηλώσεις

ELSEVIER

Critical Reviews in Oncology/Hematology 82 (2012) 51–77

CRITICAL REVIEWS IN Oncology Hematology Incorporating Geriatric Oncology

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Chemotherapy-induced peripheral neurotoxicity (CIPN): An update

Andreas A. Argyriou[a], Jordi Bruna[b,c], Paola Marmiroli[d], Guido Cavaletti[d,*]

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Accepted 28 April 2011

Drug	Sensory	Motor	Reflexes	Autonomic
Platinum compounds				
Cisplatin	30–40% of patients. Distal predominant, symmetric, upper and lower limb loss of all modalities (large fiber greater than small fiber). May progress for several months after drug discontinued. Pain is common	Normal	Reduced in proportion to sensory loss	Rare
Carboplatin	10–20% of patients. Similar but less prominent than cisplatin. Pain is less common than with cisplatin	Normal	Similar to cisplatin	Rare
Oxaliplatin (acute)	80% of patients. Cold-induced dysesthesia in mouth, throat, and upper limbs	Cramps and/or muscle spasms in throat muscles	No changes	None
Oxaliplatin (chronic)	Similar to cisplatin	Normal	Similar to cisplatin	Rare
Vinca alkaloids				
Vincristine, vindesine, vinblastine, vinorelbine	30–40% of patients. Distal sensory loss to all modalities in the lower limbs. Uncommon to affect upper limbs	5–10% of patients. Distal symmetric weakness in lower limbs progressing to foot drop	Early reduction or absence	Constipation common; orthostatic hypotension, less common
Taxanes				
Docetaxel, paclitaxel	10–20% of patients. Mild distal loss of all modalities in feet	Uncommon, mild weakness in foot muscles	Reduced ankle reflexes	Rare
Other agents				
Suramin	30% of patients. Distal symmetric loss of all modalities in the lower limbs	10–20% of patients. Mild distal weakness in lower limbs. Rarely, severe, subacute, distal, and proximal weakness	Reduced in proportion to weakness	Rare
Bortezomid	30–40% of patients. Mild to moderate, distal symmetric loss of all modalities in the lower limbs	5–10% of patients. Mild distal weakness in lower limbs. Rare, severe distal weakness	Reduced in proportion to sensory loss	Rare
Thalidomide	20–40% of patients. Mild to moderate, distal symmetric loss of all modalities in the lower limbs	Weakness rare	Reduced in proportion to sensory loss	Rare

Polyneuropathy ("glove and stocking" deficits)

Windebank et al. 2008

Παράγοντες βαρύτητας CIPN

asymptomatic	symptomatic
Reversible	irreversible
Preventable	not preventable
Treatable	untreatable
Non cumulative	cumulative
Non-’coasting’	‘coasting’

Το κακό παράδειγμα της ΟΧΑ

asymptomatic	symptomatic
Reversible	irreversible
Preventable	not preventable
Treatable	untreatable
Non cumulative	cumulative
Non-’coasting’	‘coasting’

- Οξεία παροδική νευροτοξικότητα που επάγεται από το κρύο σαν νευρομυοτονία, αποτέλεσμα διαυλοπάθειας (διαύλους Να)

Level of evidence

JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline

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Clinical Practice Guideline Committee approval: November 19, 2013.

Editor's note: This American Society of Clinical Oncology Clinical Practice Guideline provides recommendations with review and analyses of the relevant literature for each recommendation. Additional information, which may

A B S T R A C T

Purpose
To provide evidence-based guidance on the optimum prevention and treatment approaches in the management of chemotherapy-induced peripheral neuropathies (CIPN) in adult cancer survivors.

Methods
A systematic literature search identified relevant, randomized controlled trials (RCTs) for the treatment of CIPN. Primary outcomes included incidence and severity of neuropathy as measured by neurophysiologic changes, patient-reported outcomes, and quality of life.

Results
A total of 48 RCTs met eligibility criteria and comprise the evidentiary basis for the recommendations. Trials tended to be small and heterogeneous, many with insufficient sample sizes to detect clinically important differences in outcomes. Primary outcomes varied across the trials, and in most cases, studies were not directly comparable because of different outcomes, measurements, and instruments used at different time points. The strength of the recommendations is based on the quality, amount, and consistency of the evidence and the balance between benefits and harms.

Recommendations:
On the basis of the paucity of high-quality, consistent evidence, there are no agents recommended for the prevention of CIPN. With regard to the treatment of existing CIPN, the best available data support a moderate recommendation for treatment with duloxetine. Although the CIPN trials are inconclusive regarding tricyclic antidepressants (such as nortriptyline), gabapentin, and a compounded topical gel containing baclofen, amitriptyline HCL, and ketamine, these agents may be offered on the basis of data supporting their utility in other neuropathic pain conditions given the limited other CIPN treatment options. Further research on these agents is warranted.

Clinical Research Practices

Guideline Summary

Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: American Society of Clinical Oncology Clinical Practice Guideline Summary

Dawn L. Hershman, MD, MS, Christina Lacchetti, MHSc, and Charles L. Loprinzi, MD

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See accompanying article in *J Clin Oncol* doi: 10.1200/JCO.2013.54.0914

THE BOTTOM LINE

GUIDELINE QUESTION

What are the optimum prevention and treatment approaches in the management of chemotherapy-induced neuropathies in adult cancer survivors?

Target Population
- Adult cancer survivors with chemotherapy-induced neuropathies (CIPNs)

Target Audience
- Health care practitioners who provide care to cancer survivors

Recommendations
- The following recommendations are evidence based, informed by small randomized controlled trials, and guided by clinical experience. The recommendations were developed by a multidisciplinary group of experts. Ratings for benefits, harms, evidence quality, and recommendation strength are provided in Table 3 (see Appendix Table A1, online only, for rating definitions).

Prevention of CIPN
- There are no established agents recommended for the prevention of CIPN in patients with cancer undergoing treatment with neurotoxic agents. This is based on the paucity of high-quality, consistent evidence and a balance of benefits versus harms.
- Clinicians should not offer the following agents for the prevention of CIPN to patients with cancer undergoing treatment with neurotoxic agents:
  - Acetyl-L-carnitine (ALC)
  - Amifostine
  - Amitriptyline
  - CaMg for patients receiving oxaliplatin-based chemotherapy
  - Diethyldithio-carbamate (DDTC)
  - Glutathione (GSH) for patients receiving paclitaxel/carboplatin chemotherapy
  - Nimodipine
  - Org 2766
  - All-*trans*-retinoic acid
  - rhuLIF
  - Vitamin E

  Venlafaxine is not recommended for routine use in clinical practice. Although the venlafaxine data support its potential utility, the data were not strong enough to recommend its use in clinical practice, until additional supporting data become available.
  No recommendations can be made on the use of *N*-acetylcysteine, carbamazepine, glutamate, GSH for patients receiving cisplatin or oxaliplatin-based chemotherapy, goshajinkigan (GJG), omega-3 fatty acids, or oxycarbazepine for the prevention of CIPN at this time.

42 RCTs

Treatment of CIPN
- For patients with cancer experiencing CIPN, clinicians may offer duloxetine
  No recommendations can be made on the use of:
- ALC, noting that a positive phase III abstract supported its value, but this work has not yet been published in a peer-reviewed journal, and a prevention trial suggested that this agent was associated with worse outcomes.
- Tricyclic antidepressants; however, based on the limited options that are available for this prominent clinical problem and the demonstrated efficacy of these drugs for other neuropathic pain conditions, it is reasonable to try a tricyclic antidepressant (eg, nortriptyline or desipramine) in patients suffering from CIPN after a discussion with the patients about the limited scientific evidence for CIPN, potential harms, benefits, cost, and patient preferences.
- Gabapentin, noting that the available data were limited regarding its efficacy for treating CIPN. However, the panel felt that this agent is reasonable to try for selected patients with CIPN pain given that only a single negative randomized trial for this agent was completed, the established efficacy of gabapentin and pregabalin for other forms of neuropathic pain, and the limited CIPN treatment options. Patients should be informed about the limited scientific evidence for CIPN, potential harms, benefits, and costs.

6 RCTS

- A topical gel treatment containing baclofen (10 mg), amitriptyline HCL (40 mg), and ketamine (20 mg), noting that a single trial indicated that this product did decrease CIPN symptoms. Given the available data, the panel felt that this agent is reasonable to try for selected patients with CIPN pain. Patients should be informed about the limited scientific evidence for the treatment of CIPN, potential harms, benefits, and costs.

Note: The guide for rating recommendations and strength of evidence is provided in Appendix Table A1 (online only).

ASCO special articles

Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: ASCO Guideline Update

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abstract

PURPOSE To update the ASCO guideline on the recommended prevention and treatment approaches in the management of chemotherapy-induced peripheral neuropathy (CIPN) in adult cancer survivors.

METHODS An Expert Panel conducted targeted systematic literature reviews to identify new studies.

RESULTS The search strategy identified 257 new references, which led to a full-text review of 87 manuscripts. A total of 3 systematic reviews, 2 with meta-analyses, and 28 primary trials for prevention of CIPN in addition to 14 primary trials related to treatment of established CIPN, are included in this update.

RECOMMENDATIONS The identified data reconfirmed that no agents are recommended for the prevention of CIPN. The use of acetyl-L-carnitine for the prevention of CIPN in patients with cancer should be discouraged. Furthermore, clinicians should assess the appropriateness of dose delaying, dose reduction, substitutions, or stopping chemotherapy in patients who develop intolerable neuropathy and/or functional impairment. Duloxetine is the only agent that has appropriate evidence to support its use for patients with established painful CIPN. Nonetheless, the amount of benefit from duloxetine is limited.

Additional information is available at www.asco.org/survivorship-guidelines.

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WILEY

REVIEW

Immune checkpoint inhibitors-induced neuromuscular toxicity: From pathogenesis to treatment

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Abstract

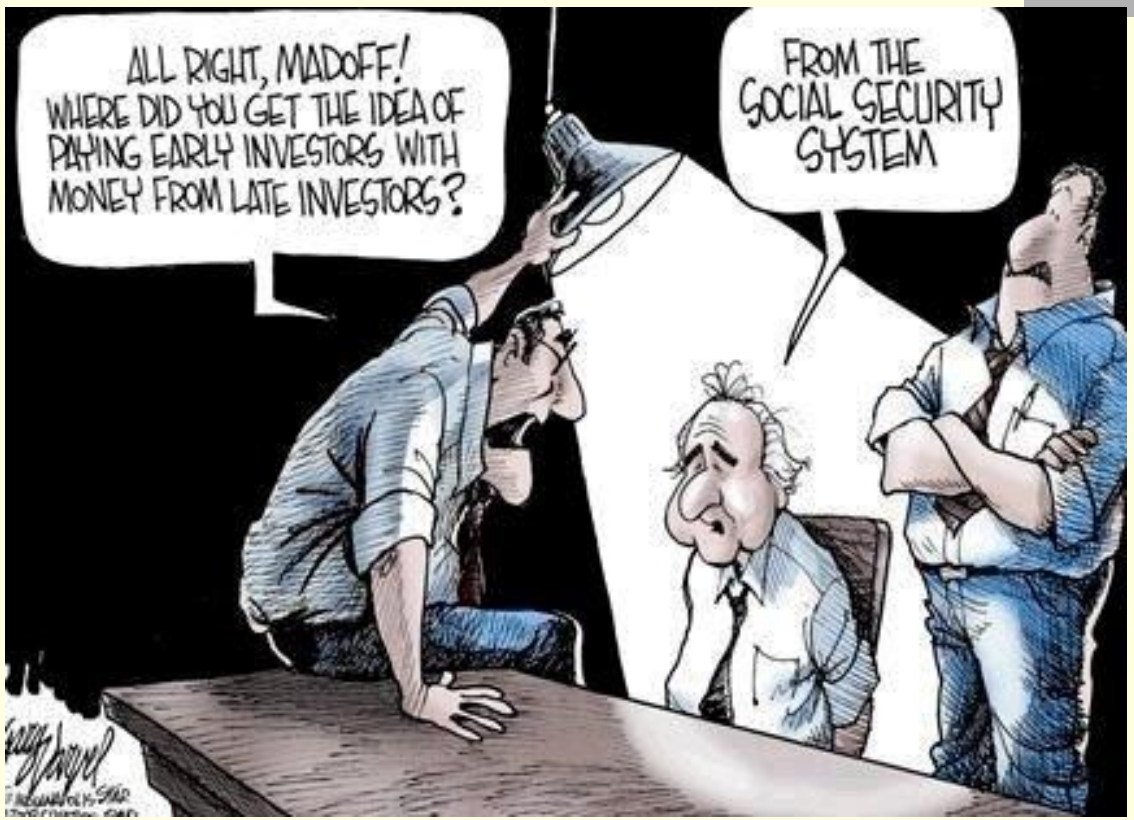
Immune checkpoint inhibitors (ICIs) are increasingly used and are becoming the standard of care in the treatment of various tumor types. Despite the favorable results in terms of oncological outcomes, these treatments have been associated with a variety of immune-related adverse events (irAEs). Neurological irAEs are rare but potentially severe. Neuromuscular disorders represent the most common neurological irAEs following anti-PD-1, anti-PD-L1, and anti-CTLA-4 treatment, and include myositis, myasthenia gravis, and demyelinating polyradiculoneuropathy. Instrumental findings may differ from typical neuromuscular disorders occurring outside ICIs treatment. Despite initial severity, neurological irAEs often respond to immune-modulating therapies. Prompt irAEs diagnosis, ICIs discontinuation, and early treatment with corticosteroids, together with patient education and a multi-disciplinary approach, are important for optimizing clinical outcomes. Intravenous immunoglobulin, plasma exchange, and other immune-modulating treatments should be considered in more severe cases. Consideration of re-challenging with the same immunotherapy drug may be given in some cases, based on clinical picture and initial severity of irAEs.

KEYWORDS

CTLA-4, demyelinating polyradiculoneuropathy, immune checkpoint inhibitor, myasthenia gravis, myositis, nivolumab, PD-1, PD-L1, pembrolizumab, peripheral neuropathy

Ευχαριστώ για την προσοχή σας!!

Και παρακαλώ…



…για τις ερωτήσεις σας