Tossicità neurologica da antiblastici

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Asco 2015-educational book

Chemotherapy-Induced Peripheral Neurotoxicity in Cancer Survivors: An Underdiagnosed Clinical Entity?

Guido Cavaletti, MD, Paola Alberti, MD, and Paola Marmiroli, MD

Asco 2015

Systemic chemotherapy is a cornerstone of the modern medical management of cancer, although its use is limited by toxicity on normal tissues and organs, including the nervous system. Long-surviving or cured people strongly require a high level of wellness in addition to prolongation of life (the concept of the quality of survival), but neurologic dysfunction can severely affect daily life activities. Chemotherapy-related peripheral neurotoxicity is becoming one of the most worrisome long-term side effects in patients affected by a neoplasm. The central nervous system has a limited capacity to recover from injuries, and it is not surprising that severe damage can determine long-term or permanent neurologic dysfunction. However, the peripheral nervous system also can be permanently damaged by anticancer treatments despite its better regeneration capacities, and the effect on patients' daily life activities might be extremely severe. However, only recently, the paradigms of peripheral neurotoxicity reversibility have been scientifically challenged, and studies have been performed to capture the patients' perspectives on this issue and to measure the effect of peripheral neurotoxicity on their daily life activities. Despite these efforts, knowledge about this problem is still largely incomplete, and further studies are necessary to clarify the several still-unsettled aspects of long-term peripheral neurotoxicity of conventional and targeted anticancer chemotherapy.

Neuropatia da antiblastici e lungo-sopravviventi

CA CANCER J CLIN 2013;63:419–437

Chemotherapy-Induced Peripheral Neurotoxicity: A Critical Analysis

Susanna B. Park, PhD[1,2]*; David Goldstein, FRACP[3]; Arun V. Krishnan, FRACP, PhD[4]; Cindy S-Y Lin, PhD[5]; Michael L. Friedlander, FRACP, PhD[6]; James Cassidy, MD, PhD[7]; Martin Koltzenburg, MD, FRCP[8]; Matthew C. Kiernan, FRACP, DSc[9]

With a 3-fold increase in the number of cancer survivors noted since the 1970s, there are now over 28 million cancer survivors worldwide. Accordingly, there is a heightened awareness of long-term toxicities and the impact on quality of life following treatment in cancer survivors. This review will address the increasing importance and challenge of chemotherapy-induced neurotoxicity, with a focus on neuropathy associated with the treatment of breast cancer, colorectal cancer, testicular cancer, and hematological cancers. An overview of the diagnosis, symptomatology, and pathophysiology of chemotherapy-induced peripheral neuropathy will be provided, with a critical analysis of assessment strategies, neuroprotective approaches, and potential treatments. The review will concentrate on neuropathy associated with taxanes, platinum compounds, vinca alkaloids, thalidomide, and bortezomib, providing clinical information specific to these chemotherapies. **CA Cancer J Clin 2013;63:419–437.**

Antiblastici e neuropatia

Ca Cancer J Clin 2013 S.Park et al

TABLE 1. Chemotherapies Associated With Peripheral Neuropathy[a]

TYPE	CLASS	THRESHOLD DOSE	SENSORY NEUROPATHY	MOTOR NEUROPATHY	AUTONOMIC NEUROPATHY
Paclitaxel	Taxane	>300 mg/m^2	Predominantly sensory neuropathy	At higher doses, myalgia and myopathy	Rare
Docetaxel	Taxane	>100 mg/m^2	Predominantly sensory neuropathy	At higher doses, myalgia and myopathy	Rare
Oxaliplatin	Platinum	>550 mg/m^2	Acute sensory symptoms and chronic sensory neuropathy	Acute cramps and fasciculations	Rare
Cisplatin	Platinum	>350 mg/m^2	Predominantly sensory neuropathy	Rare	Rare
Vincristine	Vinca alkaloid	>2-6 mg/m^2	Sensory neuropathy	Muscle cramps and mild distal weakness	Yes
Thalidomide	Immunomodulatory/ antiangiogenic agent	>20 g	Sensory neuropathy	Mild distal weakness and cramps	Rare
Bortezomib	Proteasome inhibitor	>16 mg/m^2	Painful, small-fiber sensory neuropathy	Rare	Yes

[a]Treatments associated with chemotherapy-induced peripheral neuropathy and details of clinical presentations are shown, with an indication of the frequency of the presentation in sensory, motor, and autonomic neuropathy categories.

Fattori di rischio correlati alla somministrazione

FACTOR	CONSENSUS	CHEMOTHERAPY
Single dose level	Increased single doses are associated with greater neurotoxicity	• Taxanes • Oxaliplatin • Cisplatin • Vincristine • Thalidomide • Bortezomib
Cumulative dose level	Increased cumulative doses are associated with greater neurotoxicity	• Taxanes • Oxaliplatin • Cisplatin • Vincristine
	Lack of consensus regarding the relationship between cumulative dose and neurotoxicity	• Thalidomide
	Dose threshold relationship, increasing risk until a plateau at 40 to 45 mg/m^2	• Bortezomib
Infusion duration	Longer infusion duration may reduce neurotoxicity	• Taxanes • Oxaliplatin
Treatment duration	Longer duration of treatment increases the risk of neurotoxicity	• Thalidomide
	"Stop-and-go" regimens may be associated with lower neurotoxicity	• Oxaliplatin

CTCAE in the pocket

Traduzione italiana del

Common Terminology Criteria for Adverse Events

Versione 4.03

Disturbi del sistema nervoso

22

Evento avverso	Grado 1	Grado 2	Grado 3	Grado 4	Grado 5	Cod. MedDRA
Neuropatia sensoriale periferica	Asintomatica; perdita dei riflessi tendinei profondi o parestesie	Sintomi moderati; limitazione delle attività quotidiane non di cura della persona (instrumental ADL, nota 1)	Gravi sintomi; limitazione delle attività quotidiane di cura della persona (self care ADL, nota 2)	Conseguenze potenzialmente letali; è indicato un intervento urgente	Decesso	10034620
Neuropatia periferica motoria	Asintomatica; solo osservazione clinico-diagnostica; non indicato intervento	Sintomi moderati; limitazione delle attività quotidiane non di cura della persona (instrumental ADL, nota 1)	Gravi sintomi; limitazione delle attività quotidiane di cura della persona (self care ADL, nota 2); indicato dispositivo ausiliario	Conseguenze potenzialmente letali; è indicato un intervento urgente	Decesso	10034580

Attività della vita quotidiana (ADL)

* Nota 1: Instrumental ADL – attività strumentali della vita quotidiana quali preparare i pasti, fare la spesa o acquistare vestiti, usare il telefono, gestire il denaro, ecc.

** Nota 2: Self-care ADL – attività della vita quotidiana relative alla cura della persona, come: lavarsi, vestirsi e svestirsi, alimentarsi autonomamente, andare alla toilette, prendere i farmaci e non essere costretti a letto.

TABLE 2. Assessment of CIPN Via Neuropathy Grading Scales

GRADE		0	1	2	3	4
NCI Common Terminology Criteria for Adverse Events[49]	Neuropathy Sensory Subscale	None	Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function	Sensory alteration or paresthesia (including tingling), interfering with ADL	Sensory alteration or paresthesia interfering with ADL	Disabling
Total Neuropathy Score[52-54] (developed by Johns Hopkins University)	Sensory symptoms	None	Symptoms limited to fingers or toes	Symptoms extend to ankle or wrist	Symptoms extend to knee or elbow	Symptoms above knees or elbows, or functionally disabling
	Motor symptoms	None	Slight difficulty	Moderate difficulty	Require help/assistance	Paralysis
	Autonomic symptoms	0	1	2	3	4 or 5
	Pin sensibility	Normal	Reduced in fingers/toes	Reduced to wrist/ankle	Reduced to elbow/knee	Reduced to above elbow/knee
	Vibration sensibility	Normal	Reduced in fingers/toes	Reduced to wrist/ankle	Reduced to elbow/knee	Reduced to above elbow/knee
	Strength	Normal	Mild weakness	Moderate weakness	Severe weakness	Paralysis
	Deep tendon reflexes	Normal	Ankle reflex reduced	Ankle reflex absent	Ankle reflex absent, others reduced	All reflexes absent
	Sural amplitude	Normal/reduced to <5% of LLN	76%-95% LLN	51%-75% LLN	26%-50% LLN	0%-25% LLN
	Peroneal amplitude	Normal/reduced to <5% of LLN	76%-95% LLN	51%-75% LLN	26%-50% LLN	0%-25% LLN
	Vibration sensation	Normal to 125% of ULN	126%-150% ULN	151%-200% ULN	201%-300% ULN	>300% ULN

CIPN indicates chemotherapy-induced peripheral neuropathy; NCI, National Cancer Institute; ADL, activities of daily life; LLN, lower limit of normal; ULN, upper limit of normal.

Impatto sulla qualità della vita

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journal homepage: www.ejcancer.com

Persistence of docetaxel-induced neuropathy and impact on quality of life among breast cancer survivors

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Quanto incide a lungo termine?

Risk factors for persistent peripheral neuropathy (PN) (grades 2–4) 1–3 years after docetaxel treatment among 1031 patients with early-stage breast cancer in Denmark.

Neuropathy grades		Persistent peripheral neuropathy (PN) grades 2–4 $n = 157$ (%)	Persistent PN grades 0–1 $n = 874$ (%)	Unadjusted odds ratio (OR) (95% confidence interval (CI))	p	Fully adjusted OR for all factors (95% CI)†	p
Age	<55	78 (50)	565 (65)	1.0	0·0004	1.0	0.001
	⩾55	79 (50)	309 (35)	1.85 (1.32–2.61)		1.99 (1.35–2.95)	
Max grade of neuropathy during treatment	0	12 (8)	276 (32)	1.0	<0·0001	1.0	<0.0001
	1	39 (25)	357 (41)	2.51 (1.29–4.89)		2.21 (1.12–4.39)	
	2	67 (43)	169 (19)	9.12 (4.79–17.35)		7.49 (3.86–14.55)	
	3–4	39 (25)	72 (8)	12.46 (6.20–25.01)		9.94 (4.77–20.70)	
Grade of persistent* muscle and joint pain	0–1	73 (47)	693 (79)	1.0	<0.0001	1.0	<0.0001
	2–4	81 (52)	174 (20)	4.42 (3.09–3.32)		2.89 (1.87–4.48)	
	Missing	3 (2)	7 (1)				
Grade of persistent* stomatitis	0–1	144 (92)	856 (98)	1.0	0·001	1·0	0.047
	2–4	6 (4)	5 (1)	7.13 (2.15–23.68)		3·88 (1·02–14·76)	
	Missing	7 (4)	13 (1)				
Grade of persistent* fatigue	0–1	90 (57)	742 (85)	1.0	<0.0001	1.0	0.001
	2–4	64 (41)	126 (14)	4.19 (2.89–6.07)		2.19 (1.37–3.48)	
	Missing	3 (2)	6 (1)				

* Persistent; at completion of the questionnaire from one to three years after docetaxel.

† Adjusted for age, max grade of PN during treatment, grade of persistent muscle and joint pain, persistent stomatitis and persistent fatigue.

Antiblastici e neuropatia.1

da Cavalletti Asco 2015

Cisplatin	Early reduction/loss of DTR
	Distal, symmetric, upper- and lower-limb impairment/loss of all sensory modalities
	Sensory ataxia and gait imbalance are frequent
	Neuropathic pain can be present, but it is not frequent
	Coasting* phenomenon is frequent
Carboplatin	Similar to cisplatin but milder
Oxalipatin	Acute
	Cold-induced transient paresthesias in mouth, throat, and limb extremities
	Cramps/muscle spasm in throat muscle, jaw spasm
	Chronic
	Very similar to cisplatin
Bortezomib	Reduction/loss of DTR
	Mild to moderate, distal, symmetric loss of all sensory modalities occurs. Small myelinated and unmyelinated fibers are markedly affected, leading to severe neuropathic pain.
	Mild distal weakness in lower limbs is possible

Antiblastici e neuropatia.2

da Cavalletti Asco 2015

Taxanes (paclitaxel, docetaxel)	Reduction/loss of DTR
	Myalgia syndrome is frequent (as an atypical neuropathic pain?)
	Distal, symmetric, upper and lower limb impairment/loss of all sensory modalities
	Gait unsteadiness is possible because of proprioceptive loss
	Distal, symmetric weakness in lower limbs is generally mild
Epothilones (ixabepilone, sagopilone)	Signs and symptoms are similar to taxanes, but neuropathic pain is less frequent, and recovery is reportedly faster
Vinca alkaloids (vincristine, other compounds with similar but much lower neurotoxicity)	Reduction/loss of DTR
	Neuropathic pain/paresthesia at limb extremities is relatively frequent
	Distal, symmetric, upper and lower limb impairment/loss of all sensory modalities
	Distal, symmetric weakness in lower limbs progressing to foot drop
	Autonomic symptoms (eg, orthostatic hypotension, constipation) may be severe
Thalidomide	Reduction/loss of DTR
	Relatively frequent neuropathic pain at limb extremities
	Mild to moderate, distal, symmetric loss of all sensory modalities
	Weakness is rare

Abbreviations: DTR, deep tendon reflexes.
*Coasting = worsening of signs/symptoms of neuropathy over months after drug withdrawal.

Antiblastici e neuropatia.3

da Cavalletti Asco 2015

Drug	Reported Previous Neurotoxic Treatment	Description of Peripheral Nervous System Toxicity
Alemtuzumab	None	Progressive peripheral sensorimotor radiculoneuropathy and/or myelitis
Brentuximab vedotin	Previous chemotherapy (undefined)	Peripheral sensory neuropathy: any grade in up to 66%; grade 3 in up to 8%
		Peripheral motor neuropathy: any grade in up to 11%, grade 3 in up to 7%
Carfilzomib	Lenalidomide or thalidomide	Treatment-related neuropathy: any grade in up to 17%; rarely grade 3
Ibritumomab	CVP or COP or CHOP	Paresthesias: grade 1 in up to 13%
Imatinib	Cytarabine	"Pain in limbs": any grade in up to 11%; grades 3-4 in up to 1%
Ipilipumab	Carboplatin	Guillain-Barré syndrome
Lapatinib	Taxanes, vinorelbine	"Pain in extremities": any grade in up to 13%; grade 3 in $< 1\%$
Regorafenib	Oxaliplatin	Sensory neuropathy: any grade in up to 7%; grade 3 in $< 1\%$
Rituximab	CHOP (first-line), ProMACE CytaBOM (second-line)	Guillain-Barré syndrome
	None	Guillain-Barré syndrome
Sorafenib	Previous chemotherapy (undefined)	Treatment-emergent sensory neuropathy: grades 1-2 in up to 20%
Vemurafenib	Previous chemotherapy (undefined)	Peripheral neuropathy: any grade in up to 10%; grade 3 in 1%

Test di valutazione neuropatia da CHT

original article

Annals of Oncology 0: 1–9, 2012
doi:10.1093/annonc/mds329

The chemotherapy-induced peripheral neuropathy outcome measures standardization study: from consensus to the first validity and reliability findings

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EORTC-QLQ-CIPN20

Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating and dose-limiting complication of cancer treatment. Thus far, the impact of CIPN has not been studied in a systematic clinimetric manner. The objective of the study was to select outcome measures for CIPN evaluation and to establish their validity and reproducibility in a cross-sectional multicenter study.

Patients and methods: After literature review and a consensus meeting among experts, face/content validity were obtained for the following selected scales: the National Cancer Institute-Common Toxicity Criteria (NCI-CTC), the Total Neuropathy Score clinical version (TNSc), the modified Inflammatory Neuropathy Cause and Treatment (INCAT) group sensory sumscore (mISS), the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, and CIPN20 quality-of-life measures. A total of 281 patients with stable CIPN were examined. Validity (correlation) and reliability studies were carried out.

Results: Good inter-/intra-observer scores were obtained for the TNSc, mISS, and NCI-CTC sensory/motor subscales. Test–retest values were also good for the EORTC QLQ-C30 and CIPN20. Acceptable validity scores were obtained through the correlation among the measures.

Conclusion: Good validity and reliability scores were demonstrated for the set of selected impairment and quality-of-life outcome measures in CIPN. Future studies are planned to investigate the responsiveness aspects of these measures.

CIPN_20

Sensory symptoms and problems
Tingling fingers or hands?
Tingling toes or feet?
Numbness in fingers or hands?
Numbness in toes or feet?
Aching or burning pain in fingers or hands?
Aching or burning pain in toes or feet?
Trouble standing or walking?
Trouble distinguishing temperature of hot and cold water?
Trouble hearing?
Motor scale
Cramps in hands?
Cramps in feet?
Trouble holding a pen which made writing difficult?
Trouble handling small objects (e.g. buttoning a blouse)?
Trouble opening jar or bottle due to loss of strength in hands?
Trouble walking because your feet come down to hard?
Trouble walking stairs or standing up from a chair due to weakness in legs?
Only for those driving cars: Trouble driving due to use of pedals?
Autonomic scale
Dizziness after standing up?
Blurry vision?
Only for males: Trouble getting or maintaining an erection?

Meccanismi di tossicità neurologica

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Mini review

Chemotherapy-induced peripheral neuropathy: What do we know about mechanisms?

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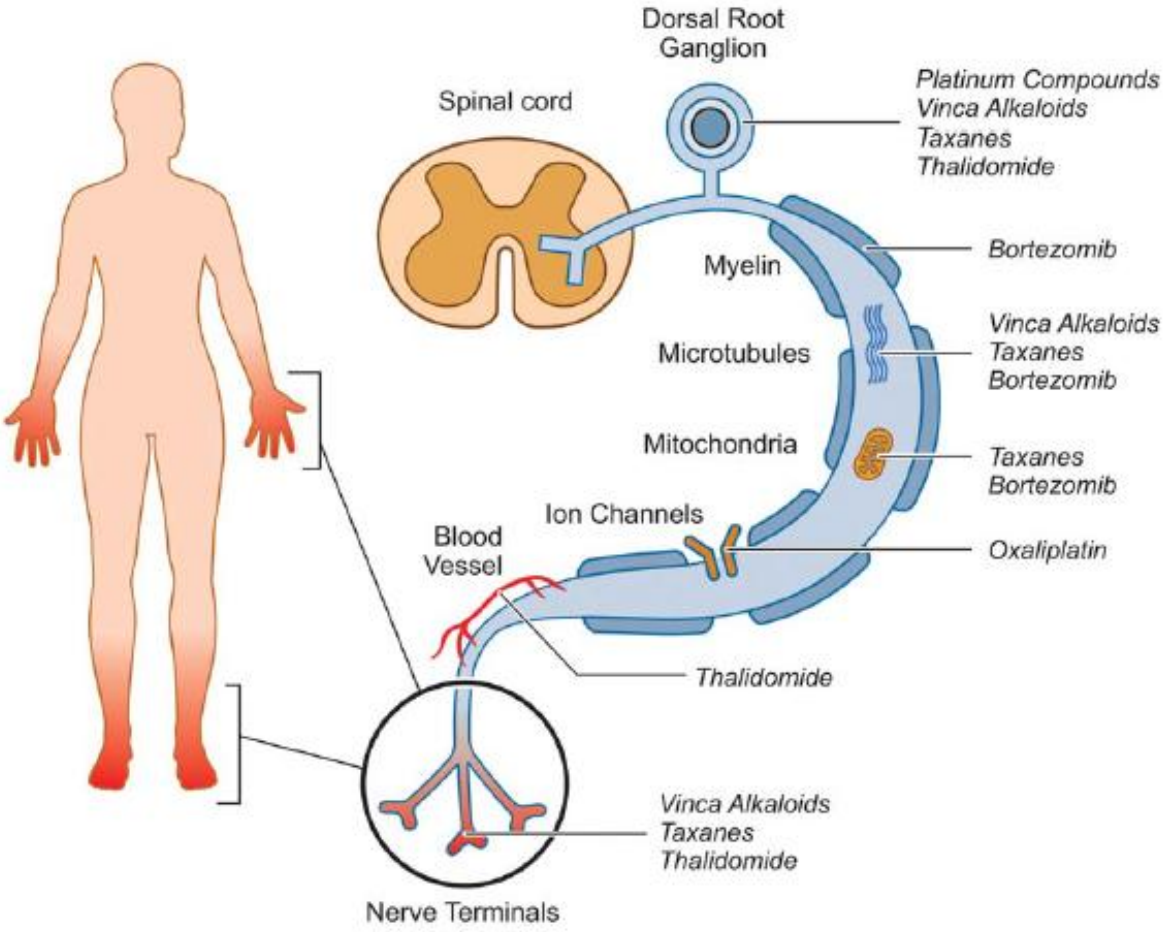
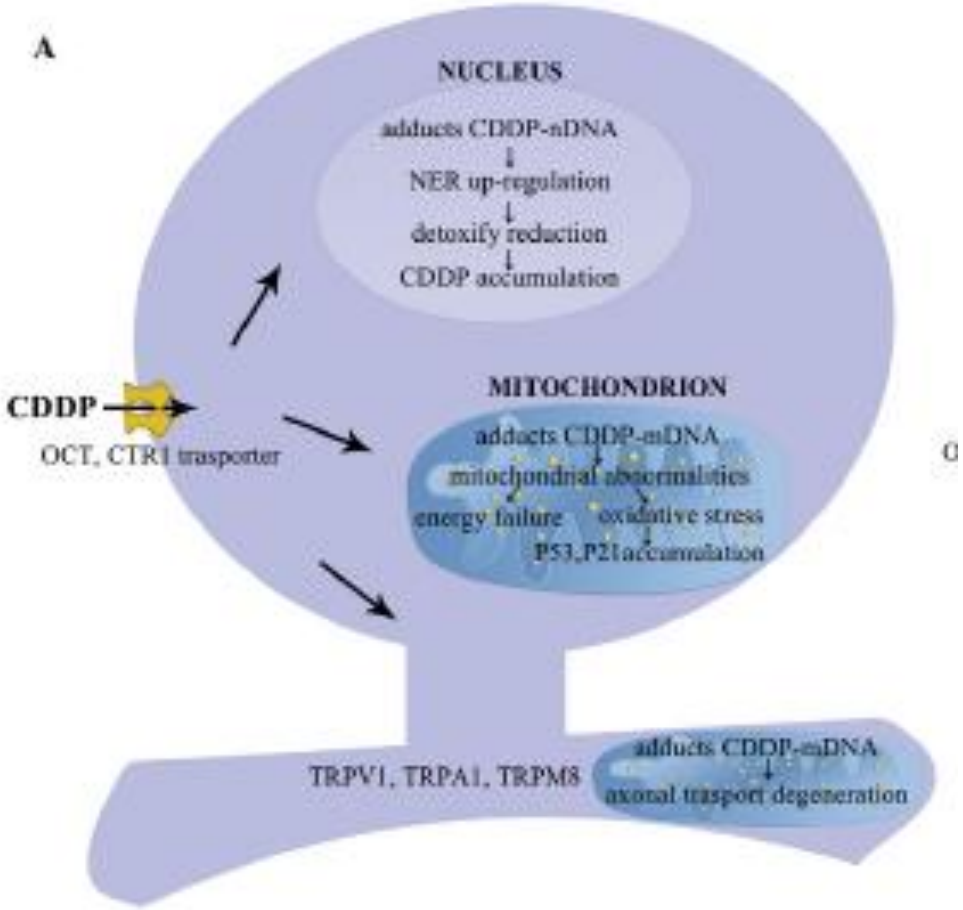
Un sistema complesso



Cisplatino

da Carozzi Neuroscience letters 2014



Oxaliplatino

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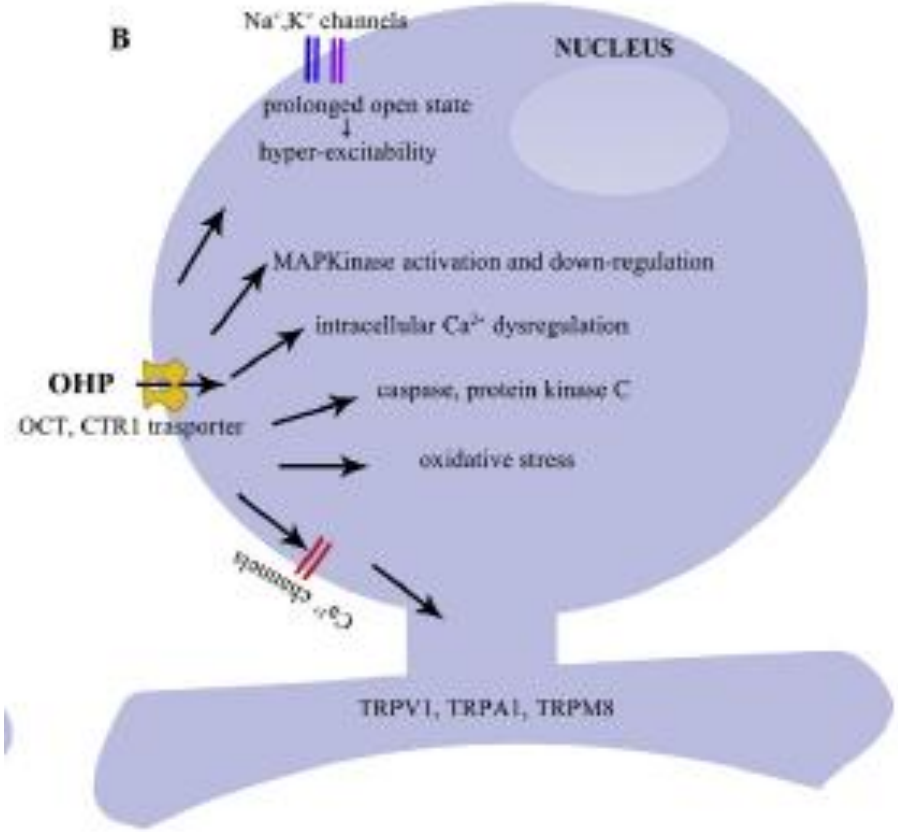

Vincristina

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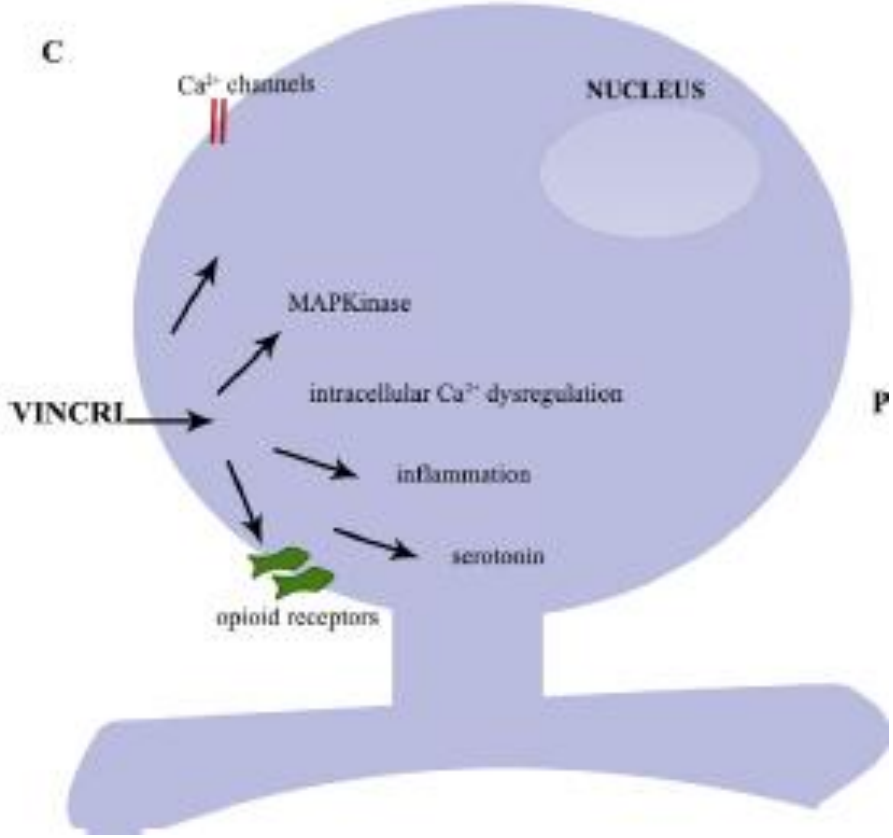

Paclitaxel

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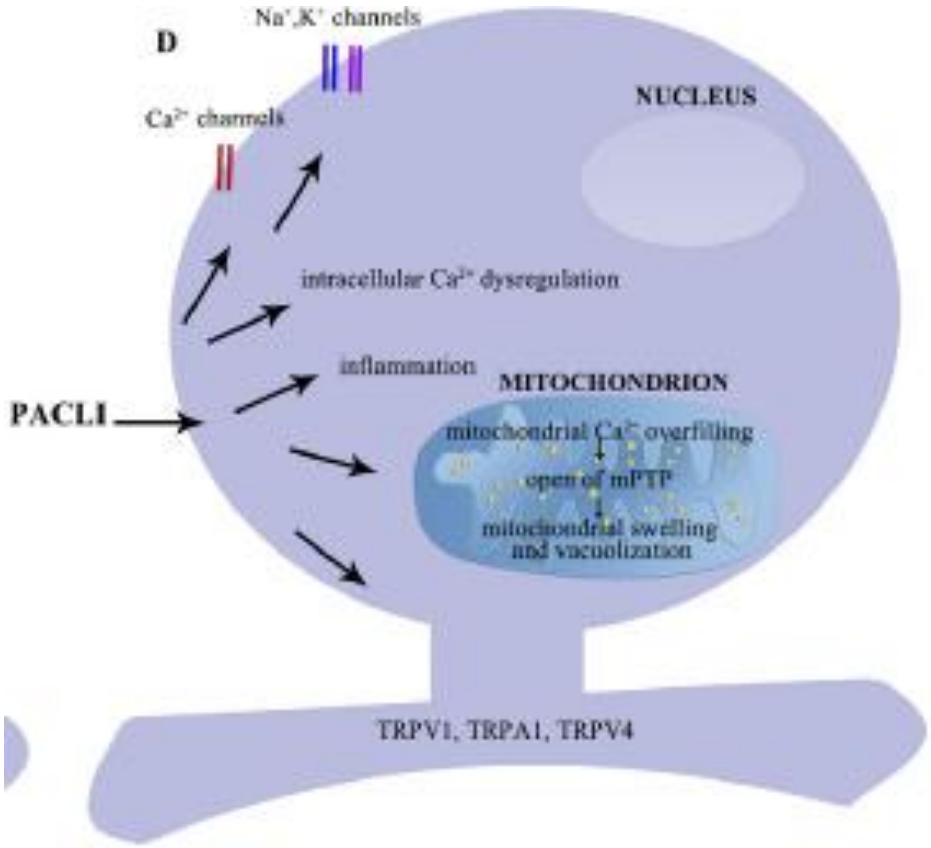

Un sistema complesso

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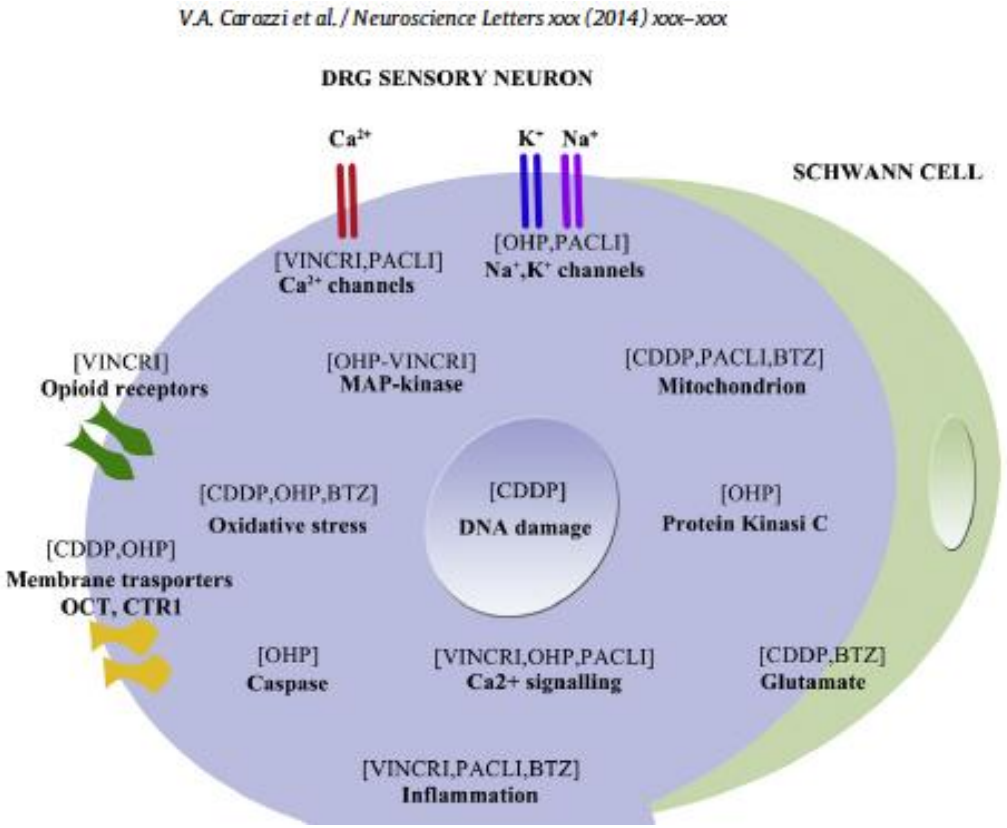

Un sistema complesso

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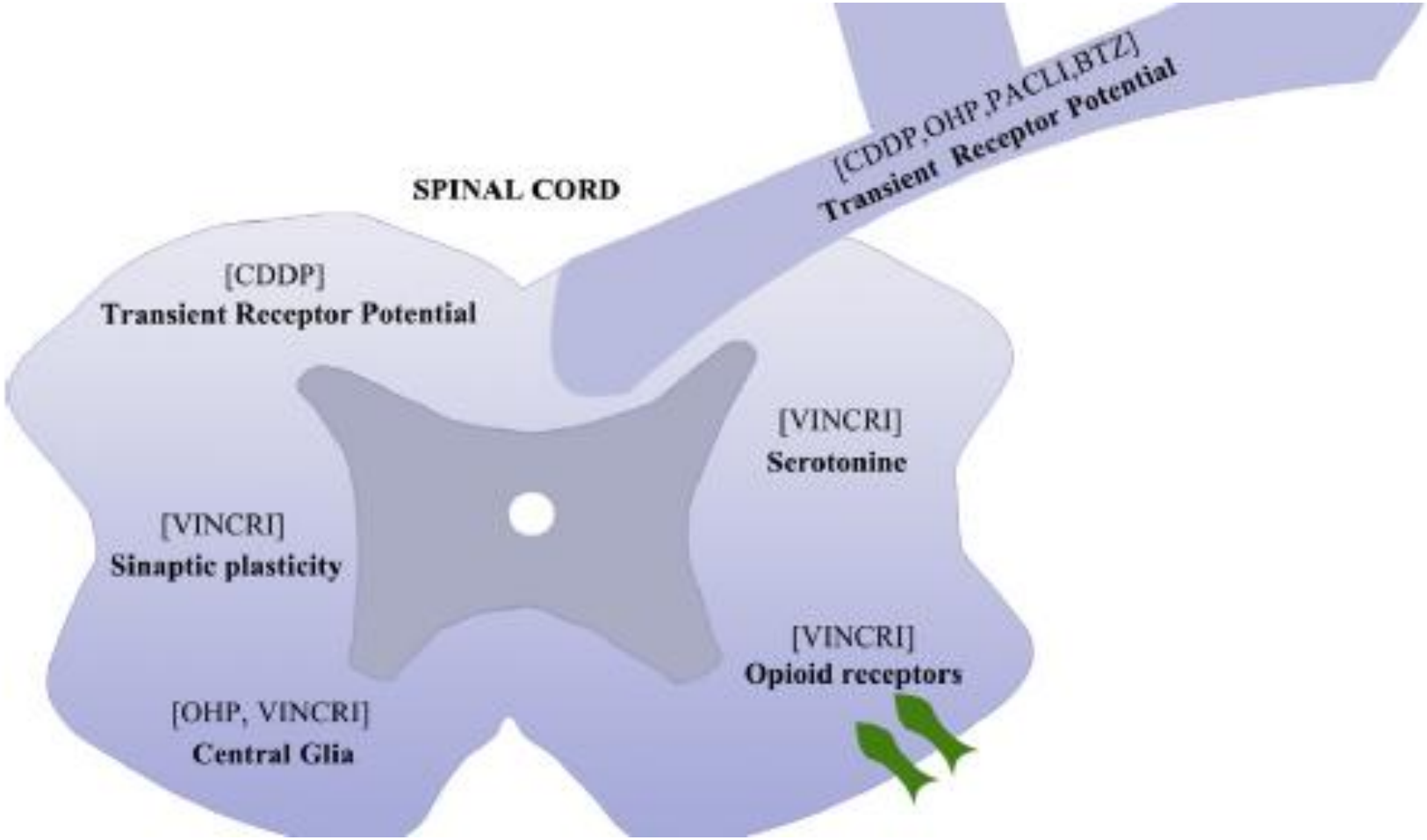

Asco guidelines 2014

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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

Dawn L. Hershman, Christina Lacchetti, Robert H. Dworkin, Ellen M. Lavoie Smith, Jonathan Bleeker, Guido Cavaletti, Cynthia Chauhan, Patrick Gavin, Antoinette Lavino, Maryam B. Lustberg, Judith Paice, Bryan Schneider, Mary Lou Smith, Tom Smith, Shelby Terstriep, Nina Wagner-Johnston, Kate Bak, and Charles L. Loprinzi

Dawn Hershman, Columbia University Medical Center, New York; Robert Dworkin, University of Rochester, Rochester, NY; Christina Lacchetti and Kate Bak, American Society of Clinical Oncology, Alexandria, VA; Ellen M

Asco guidelines 2014

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.

J Clin Oncol 32:1941-1967. © 2014 by American Society of Clinical Oncology

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Prevention of CIPN

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.

No recommendations can be made on the use of *N*-acetylcysteine, carbamazepine, glutamate, GSH for patients receiving cisplatin or oxaliplatin-based chemotherapy, goshajinkigan, omega-3 fatty acids, or oxycarbazepine for the prevention of CIPN at this time.

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Treatment of CIPN

For patients with cancer experiencing CIPN, clinicians may offer duloxetine.

No recommendations can be made on the use of:

- ALC
- Tricyclic antidepressants
- Gabapentin
- A topical gel treatment containing baclofen, amitriptyline HCL, and ketamine

Duloxetina :da usare?

Usefulness of Duloxetine for Paclitaxel-Induced Peripheral Neuropathy Treatment in Gynecological Cancer Patients

AKIKO OTAKE[1], KIYOSHI YOSHINO[1] ,YUTAKA UEDA[1], KENJIRO SAWADA[1], SEIJI MABUCHI[1], TOSHIHIRO KIMURA[1], EIJI KOBAYASHI[1], AKI ISOBE[1], TOMOMI EGAWA-TAKATA[1], SHINYA MATSUZAKI[1], MASAMI FUJITA[2] and TADASHI KIMURA[1]

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Duloxetina

Abstract. *Aim: The present study aimed at evaluating the usefulness and adverse effects of duloxetine treatment for paclitaxel-induced peripheral neuropathy in gynecological cancer patients. Patients and Methods: Medical records of gynecological cancer patients treated with duloxetine were retrospectively studied to evaluate the drug's efficacy for paclitaxel-induced peripheral neuropathy. Results: Results from 25 patients showed that an improved response was observed in 14 (56%). By univariate and multivariate analysis, the patient's age, tumor origin, regimen of chemotherapy, accumulated doses of paclitaxel or carboplatin, previous medication, maintenance dosage and timing of treatment with duloxetine were found not to be associated with the effectiveness of duloxetine treatment. Adverse effects with duloxetine were mild and well-tolerated. Conclusion: As an option, duloxetine can be effectively used for paclitaxel-induced peripheral neuropathy in patients with gynecological cancers, irrespective of patients' age, origin of the tumor, regimen of chemotherapy, or previous medication.*

Raccomandazioni

review S.Parks 2013

TABLE 5. CIPN Recommendations and Strategies[a]

	RECOMMENDATIONS AND STRATEGIES	STRENGTH OF RECOMMENDATIONS
Assessment	Standardized approach to CIPN assessment is required including: • Baseline assessment & risk profile • Long-term follow-up at >2-3 months post treatment • Inclusion of TNS or TNSc scale • Objective evidence of neurological deficits • Patient reported outcomes: validated questionnaires (FACT-GOG/Ntx, CIPN20, PNQ, CIPN-R-ODS) • NCS essential in the clinical trials setting	 B B A A A A
Identification and early detection	• Continuing patient surveillance • Patient education regarding symptoms	B
Dose modification	• Dose modification, alternative regimens and interruption most successful prevention methods • Further development of standardized dose modification guidelines	A
Neuroprotection	• Promising approaches in development • Trials must use standardised and objective assessment methods to ensure validity (TNS scale, NCS)	A
Treatment	• No proven preventative strategies or treatments • A number of approaches trialled	A
Management	Key focus in patient care: • Patient education • Interventions to mitigate falls and injury risk • Lifestyle modification and occupational therapy • Avoidance of neuropathy risk factors	B
Long-term follow-up	• Long-term neurotoxicity is underappreciated • Impacts on function and quality of life must be assessed	A

CIPN indicates chemotherapy-induced peripheral neuropathy; TNS, Total Neuropathy Score; TNSc, Total Neuropathy Score clinical version; FACT/GOG-Ntx, Functional Assessment of Cancer/Gynecologic Oncology Group-Neurotoxicity; CIPN20, European Organization for Research and Treatment of Cancer (EORTC) QLQ-CIPN20 questionnaire; PNQ, Patient Neurotoxicity Questionnaire; CIPN-R-ODS, CIPN Rasch-built Overall Disability Score; NCS, nerve conduction studies.

[a]The strength of the recommendations was identified via the Strength of Recommendation Taxonomy (SORT) algorithm, with level A evidence comprising consistent and good-quality patient-oriented evidence; level B comprising inconsistent or limited-quality patient-oriented evidence; and level C evidence comprising recommendation based on consensus, usual practice, disease-oriented evidence, case studies, or opinion.[4]

improvement in small-fiber or large-fiber nerve dysfunction at one year of follow-up,[203] indicating that clinical recovery

improvements with dose reduction protocols are not well described. Shorter treatment courses, longer infusion

Conclusioni

Educational Asco 2015

KEY POINTS

- Anticancer chemotherapy can permanently damage both the central and the peripheral nervous systems, but the mechanism(s) of this toxicity is largely unknown.
- The recognition of chemotherapy-induced peripheral neurotoxicity is simple, if education is provided and a high level of attention is maintained.
- Chemotherapy-induced peripheral neurotoxicity is probably an underestimated clinical problem in cancer survivors.
- Patients' and health-care providers' perceptions of the severity of chemotherapy-induced peripheral neurotoxicity may be very different, as demonstrated by recent studies focused on this highly relevant issue.
- No effective treatments are available for alleviating persistent symptoms of chemotherapy-induced peripheral neurotoxicity.