Randomized controlled trial of cryotherapy to prevent paclitaxel-induced peripheral neuropathy (RU221511I); an ACCRU Trial

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Introduction

It has been hypothesized that cooling the extremities during chemotherapy will reduce neurotoxicity.

Objectives

To assess if cryotherapy prevents chemotherapy-induced peripheral neuropathy.

Methods

A randomized pilot trial compared cryotherapy to standard care (control) in patients initiating paclitaxel weekly for 12 weeks. On cryotherapy, the hands and feet were cooled between 15 minutes before and 15 minutes after each paclitaxel dose. The EORTC QLQ-CIPN20 was completed at baseline and weekly through paclitaxel. The area under the curve (AUC) for CIPN20 scores was calculated using the trapezoidal rule after adjusting for baseline score and compared between arms, using the Wilcoxon rank-sum test. Cross-study comparisons were performed using data from 2 prior similarly-conducted trials (RU221408I and RC11C3).

Results

- Cryotherapy was reasonably well-tolerated (with 16 cryotherapy and 17 control patients completing study treatment)
- EORTC QLQCIPN20 data did not differ between the arms in any of the neuropathy outcomes
- When the cryotherapy arm of the current trial was compared to the combined control arms from all three trials, it appeared that there was less neuropathy in the cryotherapy arm than the combined control arms (Wilcoxon Rank Sum $p = 0.004$)

Table 1: Baseline Characteristics

	Cryotherapy (N=21)	Control (N=21)
Age Group (%)		
<=50 years	38%	43%
>50 years	62%	57%
Gender (%)		
Female	95%	100%
Male	5%	0%
Performance Score (%)		
0	86%	85.7%
1	14%	14.3%
Diabetes (%)		
Yes	0%	5%
No	100%	95%
Tumor Status (%)		
Resected with no residual	48%	76%
Unresected	48%	24%
Recurrent	5%	0%
Prior Therapy (%)		
Yes	48%	52%
No	52%	48%
Baseline CIPN20: Autonomic Score		
Mean (SD)	96 (7)	96 (10)
Motor Score		
Mean (SD)	96 (8)	97 (5)
Sensory Score		
Mean (SD)	97 (6)	97 (6)

Figure 1: Patient Consort Diagram

Figure 2: Neuropathy Scores by Trial

CIPN during 12 weeks of treatment represented as the scores the EORTC QLQ-CIPN20 sensory scores for patients participating in the current trial and in two prior trials that had evaluated minocycline and pregabalin, using virtually identical protocol methodologies. Higher scores represent fewer symptoms. Figure 2A illustrates data with the individual control arms for the 3 trials shown separately, while 2B combines the control arms into one line.

Conclusion

- While there was no difference in CIPN20 scores between the 2 study arms in the current trial, further investigation is needed
- Patients in the control arm of the current trial experienced substantially less neuropathy than did placebo recipients in two similar trials that assessed minocycline and pregabalin in this setting

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