Safety and efficacy of desensitization protocols for platinum hypersensitivity reactions

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Objectives

- To examine the relative safety of desensitization protocols on patients receiving oxaliplatin and carboplatin at Mayo Clinic, Rochester.
- To describe the timing and pattern of reactions while on desensitization protocols.
- To determine if a potential "low-risk" cohort exists for future prospective study of returning to outpatient setting with simplified treatment protocol.

Table 2: Demographic information

	Oxaliplatin (n=20)	Carboplatin (n=34)
Median Age (range)	54 (32-69)	63 (22-73)
Sex (%)		
Male	5 (25)	2 (6)
Female	15 (75)	32 (94)
Primary Cancer		
Colon	12 (60)	-
Rectal	4 (20)	-
Pancreas	2 (10)	-
CUP	1 (5)	1 (3)
Endometrial	1 (5)	5 (15)
Ovarian	-	25 (74)
Lung	-	2 (6)
Melanoma	-	1 (3)
Median cycle of initial reaction	8 (1-20)	8 (1-24)
Total desensitization episodes	54	156
Median desensitization cycles per patient (range)	2.5 (1-7)	4 (1-14)
Regimen (%)		
FOLFOX	8 (40)	-
XELOX	1 (5)	-
FOLFOX/ bevacizumab	10 (50)	-
FOLFOX/ panitumumab	1 (5)	-
Carboplatin	-	3 (8)
Carbo/pemetrexed	-	2 (5)
Carbo/liposomal doxorubicin	-	2 (5)
Carbo/gemcitabine	-	8 (21)
Carbo/paclitaxel*	-	18 (47)
Carbo/paclitaxel/ everolimus	-	1 (3)
Carbo/paclitaxel/ bevacizumab	-	3 (8)
Carbo/pemetrexed/ bevacizumab	-	1 (3)
Treatment intent (%)		
Curative	1 (5)	4 (12)
Palliative	19 (95)	30 (88)
History of atopy (%)	12 (60)	18 (53)

* Two patients received carboplatin/paclitaxel and were subsequently changed to carboplatin/gemcitabine during course of desensitization.

Methods

- All patients getting oxaliplatin or carboplatin desensitization therapy per protocol (**table 1**) from August 1, 2010 to November 30, 2014 at Mayo Clinic, Rochester, were included in analysis.
  - Received all treatment in hospital, on oncology ward
- Patient demographics and treatment outcome were abstracted from electronic medical record (**table 2**).
  - All reactions documented were included in analysis, whether or not consistent with hypersensitivity
  - Reactions were graded on severity
    - Classed as severe reaction if: symptoms potentially life threatening, or if having chest pain, dyspnea, hypotension (systolic blood pressure ≤ 90 mmHg), or severe hypertension (systolic blood pressure ≥ 180 mmHg.)

Table 1: Desensitization Protocol

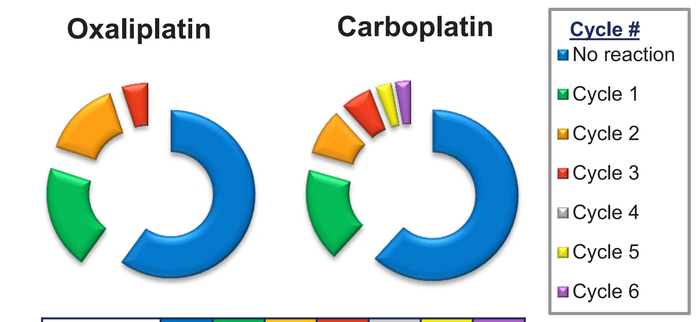
Step	Drug	Dose	Administration
1	Platinum	0.0001 mg	In 100 mL 0.9% NaCl over 15 min
2	Platinum	0.001 mg	
3	Platinum	0.01 mg	
4	Platinum	0.1 mg	
5	Platinum	24.9 mg	In 250 mL 0.9% NaCl over 3 h (carbo) or 2 h (oxali)
6	Platinum	Rest of dose	In 500 mL D5W over 4 hours

Premedications: Dexamethasone 20 mg IV once prior to start, diphenhydramine 50 mg IV at start and 25 mg IV every 4 h, famotidine 20 mg IV at start, hydrocortisone 100 mg every 4 h.

Results

- Initial hypersensitivity reactions (pre-desensitization) were most commonly cutaneous for both drugs.
  - 45% oxaliplatin (oxali) and 44% carboplatin (carbo) of initial reactions were severe
- Eight of 20 (40%) of oxali and 12/34 (35.3%) of carbo patients had reactions on desensitization protocols over 10/54 (18.5%) oxali and 21/156 (13.5%) carbo episodes.
  - Where noted, all occurred on 5th or 6th treatment step.
  - None developed reactions after 3rd oxali and 6th carbo cycle (**Figure 1**).
  - Only 1 (1.9%) oxali and 4 (2.6%) carbo reactions were severe (**Figure 2**).
    - Oxali: dyspnea, resolved with albuterol
    - Carbo: 3 cases chest pain, 1 dyspnea resulting in Rapid Response Team intervention while receiving paclitaxel portion.
    - No Intensive Care Unit (ICU) admissions or deaths
    - 2 oxali and 1 carbo doses were aborted prior to completion at provider discretion.
- Minority of patients with desensitization reaction had subsequent reaction (1/6 [16.7%] oxali, 4/13 [30.8%] carbo).

Figure 1



	No	#1	#2	#3	#4	#5	#6
Oxaliplatin	12	4	3	1	0	0	0
Carboplatin	21	6	3	2	0	1	1

Figure 1. Timing (by cycle) of first hypersensitivity reaction while receiving platinum on desensitization protocol.

Figure 2

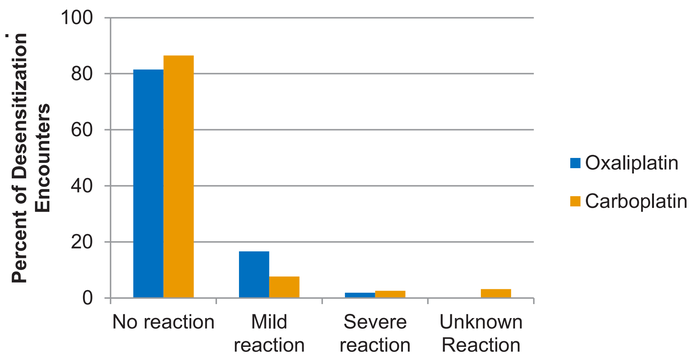


Figure 2. Severity of hypersensitivity reaction while on desensitization. The majority of patients had no reaction, and no severe reactions required ICU admission.

Conclusions

- As at other institutions[1,2,3], desensitization protocols have allowed safe administration of platinum agents.
  - ICU-level of care not necessary, unless close nurse monitoring not otherwise available.
- Oxaliplatin is associated with higher risk of having reaction while receiving desensitization, compared to carboplatin. This risk appears to extinguish more rapidly than for carboplatin.
- If an oxaliplatin hypersensitivity reaction occurs on desensitization, it will happen within the first 2-3 cycles.
  - Suggests potential "low-risk" population exists
  - Opportunity for prospective study of transitioning to more rapid desensitization or to outpatient therapy

References

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