A Real World Data Approach to Determine the Optimal Dosing Strategy for Pembrolizumab

Lynne Nakashima[1], Ashley Jang[1,2] and Tonya Ng[1]

[1]BC Cancer, Vancouver, BC, Canada, [2]University of British Columbia, Vancouver, BC, Canada

Background

Cancer drug therapy costs continue to rise and threaten the sustainability of Canada's public health care system. Previous studies have calculated potential savings utilizing different dosing regimens of cancer treatment medications.

BC Cancer is a provincial organization that coordinates and provides cancer care for patients through six regional centres located in Vancouver, Surrey, Abbotsford, Victoria, Kelowna, and Prince George, as well as a network of approximately 30 hospitals located around the province. Pembrolizumab is a high cost medication that was approved by BC Cancer for use in metastatic melanoma (June 2016) and advanced non-small cell lung cancer (NSCLC) (March 2017).

Objective

This study investigates the use of pembrolizumab through actual compared to optimal usage, wastage and cost, and compares alternative dosing regimens for potential cost-effectiveness to:

(1) Determine the financial impact of wastage on the total spend.

(2) Explore different dosing regimens to determine cost-effective alternatives considering the impact of the discontinuation of the 50 mg vial size.

Methods

Design:

- Multi-centre retrospective review of usage and wastage data

Population:

- Patients treated with pembrolizumab at any of the six BC Cancer regional centres between April 1, 2017 and March 31, 2019

Inclusion:

- Patients who received at least one dose of pembrolizumab for NSCLC or unresectable or metastatic melanoma:
  - First-Line Treatment of Advanced NSCLC (ULUAVPMBF)
    - 2 mg/kg to a maximum dose of 200 mg
  - Second- or Subsequent-Line Treatment of Advanced NSCLC (ULUAVPMB)
    - 2 mg/kg to a maximum dose of 200 mg
  - Unresectable or Metastatic Melanoma (USMAVPEM)
    - 2 mg/kg initially implemented with no maximum dose

Exclusion:

- Patients who received pembrolizumab on a clinical trial

Data Analysis:

- Centres were de-identified and assigned a letter from A to F
- Costs were calculated based on the list price as submitted to the pan-Canadian Oncology Drug Review (pCODR) of $44.00 Canadian per mg[1,2]
- Usage was determined based on Pharmacy computer records of doses dispensed and calculated based on the smallest number of vials used to minimize wastage
- Wastage was determined by the total amount of drug leftover in the vial recorded in Pharmacy wastage logs

Results

Of 553 patients identified, 384 NSCLC and melanoma patients met the criteria for eligibility shown in table 1. Five patients received treatments on both ULUAVPMBF and ULUAVPMB.

Table 1. Patient Treatment Demographics

	Melanoma	NSCLC		Total
Protocol	USMAVPEM	ULUAVPMBF	ULAVPMB	
Number of Patients	182	153	54	389
Number of Doses	1,713	964	271	2,948

Overall, drug wastage of $1,829,047.44 accounted for 8.65% of the total spend for during the study period shown in table 2 divided by fiscal year.

Table 2. Actual Usage and Wastage by Fiscal Year

Centre	Fiscal Year 2017-18		Fiscal Year 2018-19	
	Total Usage in mg	Drug Wastage in mg (% of total usage)	Total Usage in mg	Drug Wastage in mg (% of total usage)
A	25,869.95	2,521.75 (9.75)	60,635.50	8,300.50 (13.69)
B	1,897.50	328.50 (17.31)	11,646.33	1,710.83 (14.69)
C	24,096.90	1,528.50 (6.34)	43,993.23	6,670.63 (15.16)
D	13,589.80	444.20 (3.27)	43,539.85	1,615.85 (3.71)
E	38,415.80	4,055.00 (10.56)	74,602.60	6,511.00 (8.73)
F	56,487.00	2,320.00 (4.11)	85,820.70	5,562.50 (6.48)
TOTAL	160,356.95	11,197.95 (6.98)	320,238.21	30,371.31 (9.48)
COST	$7,055,705.80	$492,709.80	$14,090,481.24	$1,336,337.64

After fiscal year 2017-18, based on the data analysis, dosing for USMAVPEM was changed to 2 mg/kg to a maximum dose of 200 mg. In this year, 140 out of 937 (14.94%) doses were greater than 200 mg. Extrapolating from our data, based on the availability of the 50 mg vials, the estimated savings of this practice change was $660,000.00.

Results

Optimal amounts depict the impact of vial sharing using 50 mg vials in table 3 and 100 mg vials in table 4. Estimated amounts of drug wasted were calculated from the total amount of drug leftover in the vial assuming the smallest number of vials used to fulfill the dose:

- With vial sharing assumptions – based on the sum of doses dispensed per day at the same centre
- Without vial sharing assumptions – based on each dose

Table 3. Fiscal Years 2017-19 Optimal Wastage and Savings With Vial Sharing Using 50 mg Vials

Centre	Estimated Amount of Drug Wasted With Vial Sharing in mg (% of total usage)	Estimated Amount of Drug Wasted Without Vial Sharing in mg (% of total usage)	Drug Savings With Vial Sharing in mg (# of vials)
A	7,316.80 (8.82)	11,716.80 (13.41)	4,400 (88)
B	1,095.50 (8.66)	1,295.50 (10.12)	150 (3)
C	5,659.00 (8.63)	8,709.00 (12.70)	3,050 (61)
D	5,780.40 (9.50)	8,380.40 (13.21)	2,600 (52)
E	8,447.60 (7.62)	15,697.60 (13.29)	7,350 (147)
F	9,674.80 (6.71)	22,824.80 (14.51)	13,150 (263)
TOTAL	37,974.10 (7.96)	68,624.10 (13.52)	30,700 (614)
COST	$1,670,860.40	$3,019,460.40	$1,350,800.00

Table 4. Fiscal Years 2017-19 Optimal Wastage and Savings With Vial Sharing Using 100 mg Vials

Centre	Estimated Amount of Drug Wasted With Vial Sharing in mg (% of total usage)	Estimated Amount of Drug Wasted Without Vial Sharing in mg (% of total usage)	Drug Savings With Vial Sharing in mg (# of vials)
A	15,116.80 (16.65)	23,316.80 (23.55)	8,200 (82)
B	2,495.50 (17.83)	2,795.50 (19.55)	300 (3)
C	11,409.00 (16.00)	19,109.00 (24.19)	7,700 (77)
D	11,730.40 (17.56)	19,530.40 (26.18)	7,800 (78)
E	18,747.60 (15.47)	38,447.60 (27.29)	19,700 (197)
F	19,386.80 (12.60)	48,674.80 (26.58)	29,200 (292)
TOTAL	78,886.10 (15.23)	151,874.10 (25.70)	72,900 (729)
COST	$3,470,988.40	$6,682,460.40	$3,207,600.00

The comparison of cost-effective dosing regimens are illustrated in table 5. Dose bands of 100 mg and 200 mg were used for 2 mg/kg dosing rounding down strategies. Doses within 5% of the dose band were rounded down to 100 mg and doses greater than 5% were rounded up to 200 mg for "2 mg/kg dosing rounding down within 5%." "2 mg/kg dosing rounding down within 10%" followed the same method but rounded down within 10% instead of 5%.

Table 5. Fiscal Years 2017-19 Dosing Options and Associated Costs

Dosing Regimen	Mean Dose in mg	Mean Cost/ Dose	Percentage Variation Versus Fiscal Years 2017-19 Mean Cost/Dose	Annual Cost
Fiscal Years 2017-19	148.92	$6,552.63	0.00	$19,317,139.60
2 mg/kg Dosing (max: 200 mg)	147.21	$6,477.08	-1.15	$19,094,420.40
Flat Dosing of 200 mg	200.00	$8,800.00	+34.30	$25,942,400.00
2 mg/kg Dosing Rounding Down Within 5%	191.66	$8,432.84	+28.69	$24,860,000.00
2 mg/kg Dosing Rounding Down Within 10%	189.08	$8,319.40	+26.96	$24,525,600.00

Conclusion

- During fiscal years 2017-19, documented wastage for pembrolizumab approximated $1,829,047.44
- 100 mg vials result in over twice as much wastage compared to 50 mg vials and higher vial sharing savings
- Vial sharing could save $3,207,600.00 with 100 mg vials and $1,350,800.00 with 50 mg vials
- The most cost-effective dosing regimen was 2 mg/kg dosing to a maximum of 200 mg and the most expensive dosing regimen was flat dosing of 200 mg
- Data from fiscal year 2017-18 was significantly lower than fiscal year 2018-19 and therefore, the average annual impact of these strategies is higher than our data suggest

Results from our study hope to spark further initiatives to investigate how real world data can help maintain an accurate picture of drug usage and wastage, while finding other ways to mitigate costs.

Acknowledgements

The authors would like to acknowledge the input and support of the following individuals, without whom, this study could not have been completed:

Mayo Fung, Samarah Jiwani, Kimberly Schaff, Jennifer Cowie, Randy Goncalves, Dennis Jang, Kimberly Kuik, Sylvie Labelle and Alison Pow.

References

1. pCODR Economic Guidance Panel. pCODR Final Economic Guidance Report – Pembrolizumab (Keytruda) for Metastatic Melanoma [Internet]. Toronto: pan-Canadian Oncology Drug Review; 2015 Nov 16 [cited 2018 Jun 12]. Available from: https://cadth.ca/sites/default/files/pcodr/pcodr_pembrolizumab_keytruda_mm_fn_egr.pdf
2. pCODR Economic Guidance Panel. pCODR Final Economic Guidance Report – Pembrolizumab (Keytruda) for Non-Small Cell Lung Cancer [Internet]. Toronto: pan-Canadian Oncology Drug Review; 2016 Nov 3 [cited 2018 Jun 12]. Available from: https://cadth.ca/sites/default/files/pcodr/pcodr_pembrolizumab_keytruda_nsclc_fn_egr.pdf