



cell therapies

Initial Comparison of 3 apheresis platforms for supporting the collection of CD3+ cells for CAR-T production

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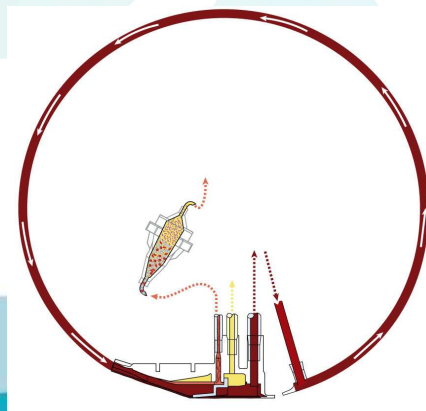
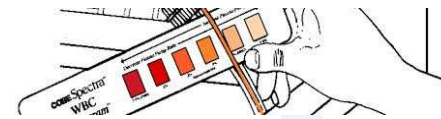


Overview

- Cobe Spectra being “retired”
- Comparison of 3 different apheresis technologies (all Terumo platforms – two Optia; one Spectra)
- Collection of CD3+ cells from steady state “healthy”/ “normal” donors
- Apheresis and cryopreservation at Peter MacCallum Cancer Centre, Melbourne

Terumo Apheresis systems

- Continuous flow Cell Separators
- Cobe Spectra – about to be retired!
- Optia MNC – dual stage, intermittent collection
- Optia cMNC



Literature

Lisenko K et al, *Journal of Clinical Apheresis*
2016 epub

Robitzsch JT et al, *BMT* 2015

Loaiza S et al, *Transfusion & Apheresis Science*
2013

Punzel M et al, *BMT 2015: 50 (Supp 1)s348*

Schulz M et al, *Transfusion* 2014: 54 (6)

Del Fante et al, *Transfusion* 2013; 53(9) 2027

Method

- Ethics approval
- Panel of donors – medical and apheresis pre-assessment, screening and consent
- Mandatory IDM, biochemistry
- FBC & Flow (CD3+ and subsets) on peripheral blood and product
- Assigned consecutively to Spectra, then Optia MNC, then Optia cMNC
- Initial processing target – 2 X TBV
- Data collected on Excel spreadsheet

Donor profile

- n = 9 (male - 8; female - 1)
- Age range - median 40 - 45
- TBV (range: 5537 - 7124mls)
- All used peripheral venous access
- All given calcium infusion (6 from start)

Collection summary

Machine	Cobe Spectra (n=3)	Optia MNC (n=3)	Optia cMNC (n=3)
Median donor TBV (mls)	6180 (5510-7124)	6438 (5787-7008)	6124 (5537 -6766)
Median run time (mins)	210 (202 – 241)	259 (230 – 262)	227 (220 – 235)
Median TBV processed (mls)	12047 (11019 – 12355)	11050 (9911 – 12291)	11833 (11074 – 13533)
Median TBV processed/ min (mls)	54.6 (51.2 – 57.4)	46.9 (38.3 – 48.0)	53.8 (48.8 – 57.6)
Median BV ratio processed	2.0 (1.7 – 2.0)	1.7 (1.7 – 1.8)	2.0 (1.9 – 2.0)
Median volume (apheresis bag)	193 (181 – 205)	100 (64 – 100)	216 (181 – 228)

Key parameters

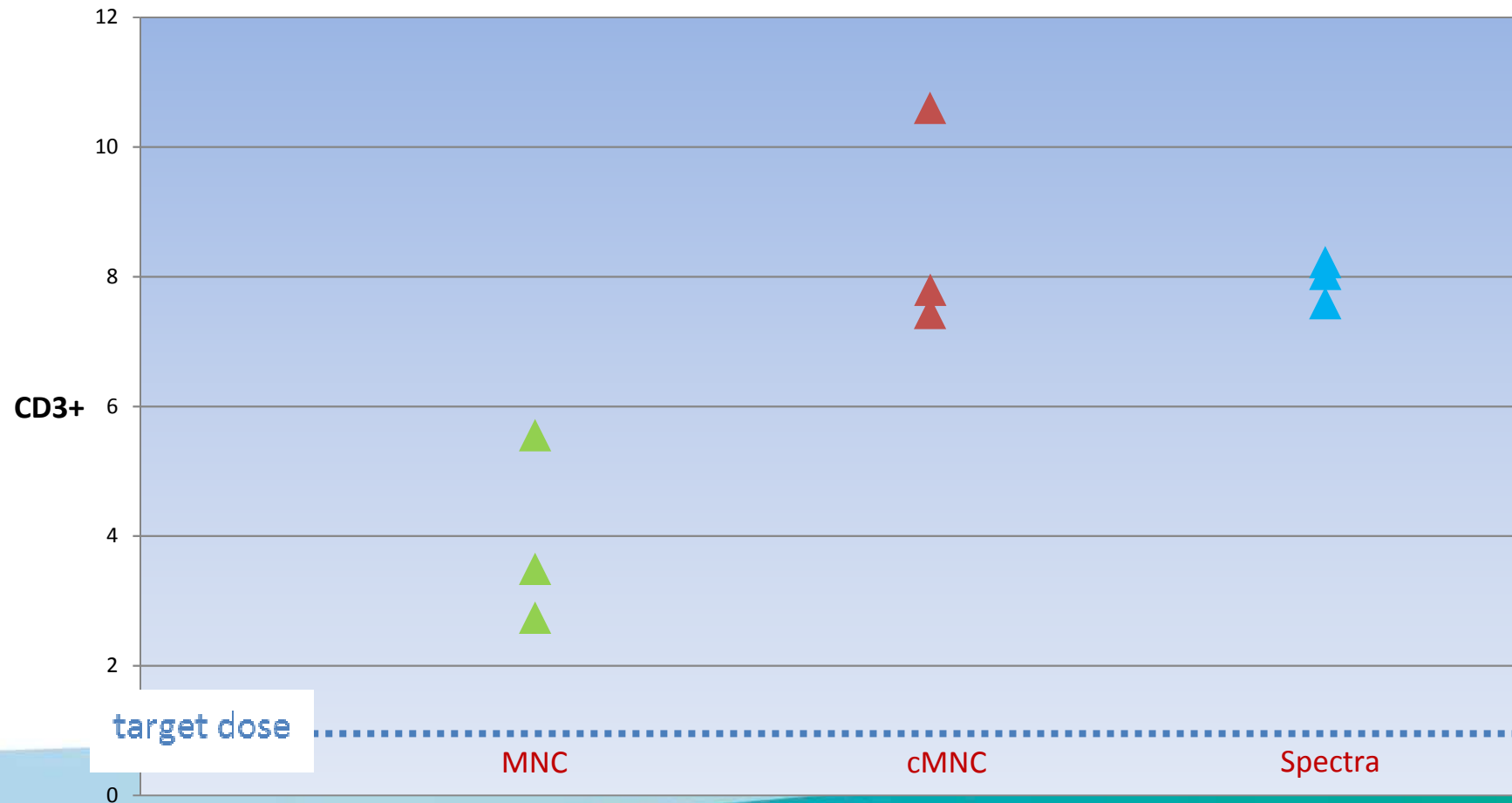
Machine	Cobe Spectra	Optia MNC	Optia cMNC
Median PB CD3+ (10 ⁶ /ml) (range)	1.25 (0.80 – 1.34)	1.10 (0.70 – 1.5)	1.10 (1.0 – 1.11)
Median TNC (range) x 10 ⁹ *	13.86 (12.87 – 22.62)	8.52 (6.30 – 10.14)	12.48 (11.80 – 17.20)
Median CD3+ (range) x 10 ⁹ *	8.04 (7.59 – 8.22)	3.50 (2.74 – 5.56)	7.80 (7.44 – 10.60)
Median CE**	58 (58 – 76)	47 (27 – 59)	76 (70 – 79)

* Targets: TNC $\geq 7 \times 10^9$ (min $\geq 2 \times 10^9$); CD3+ $\geq 1 \times 10^9$

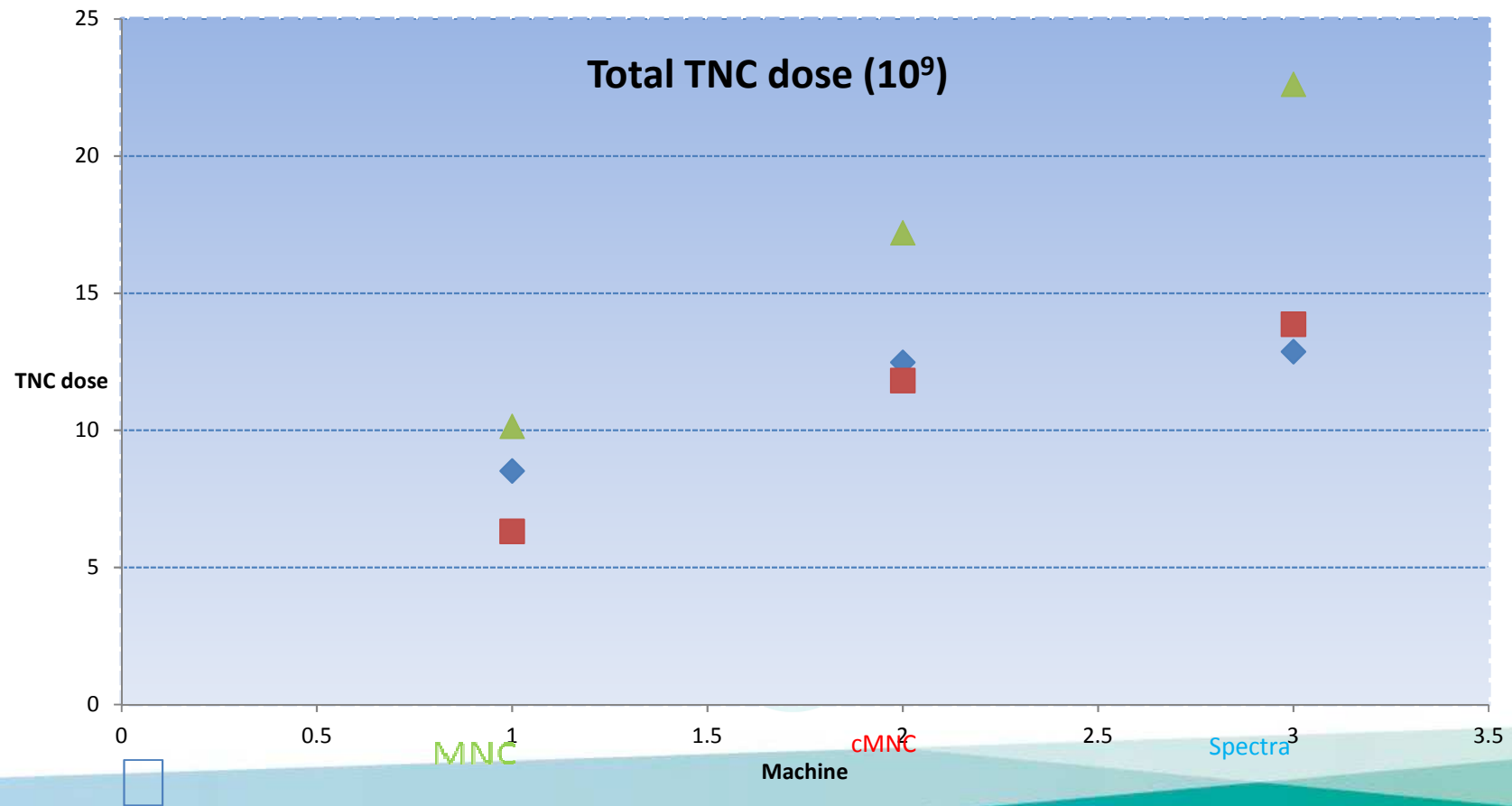
**cells collected (ml) x product volume (ml)/ CD3 pre-apheresis x vol processed

CD3+ dose

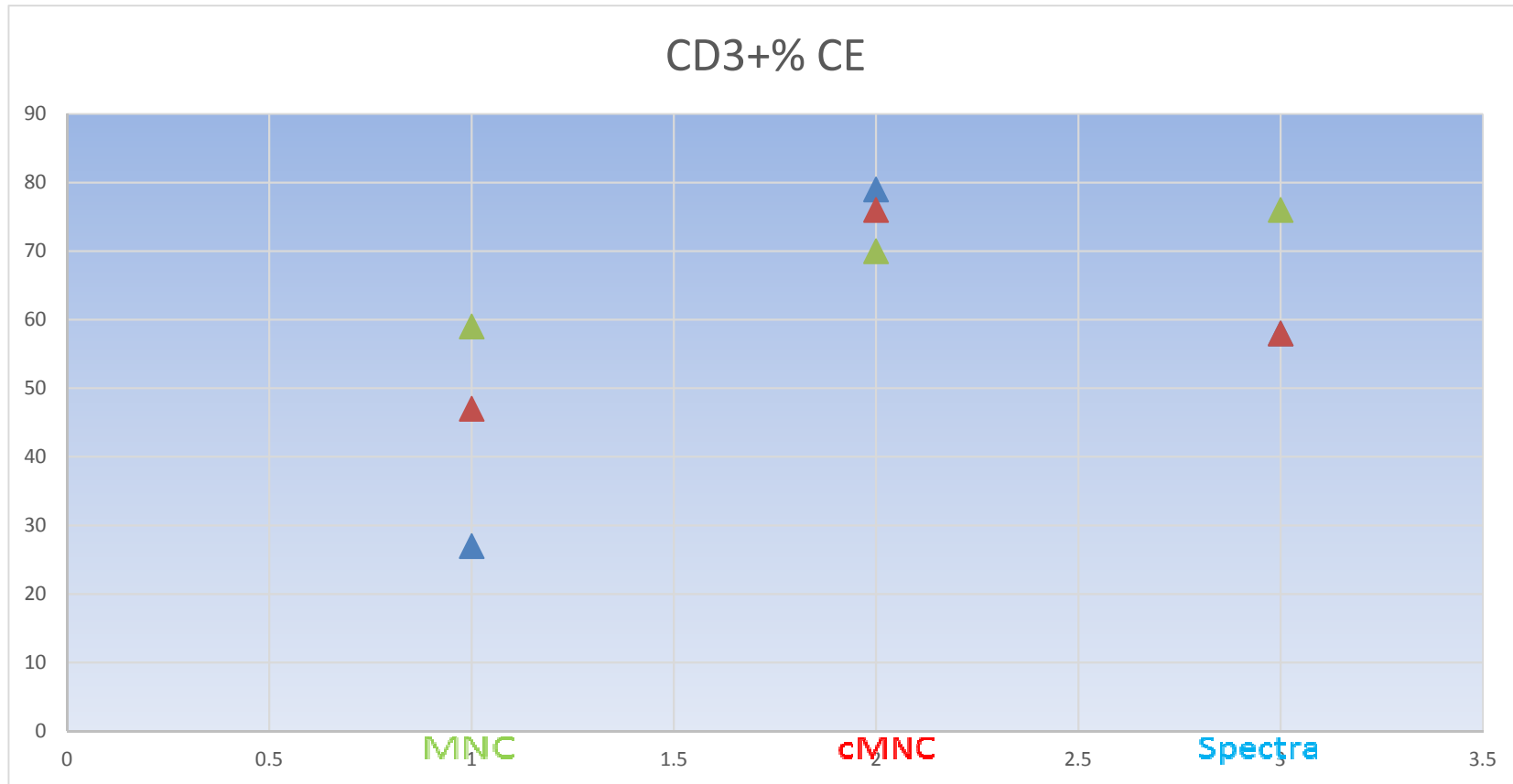
Total CD3+ dose (10^9)



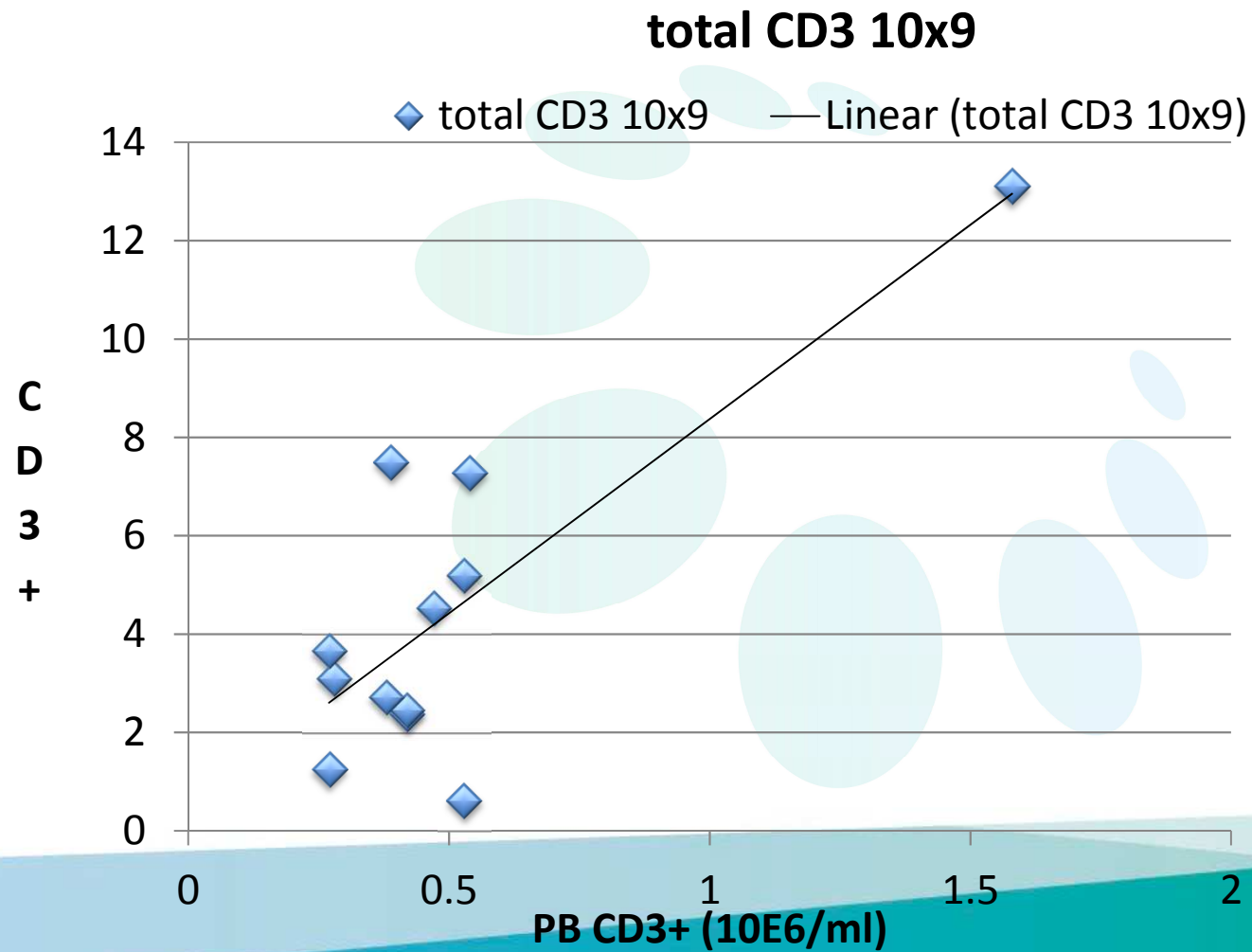
Total TNC dose (10^9)



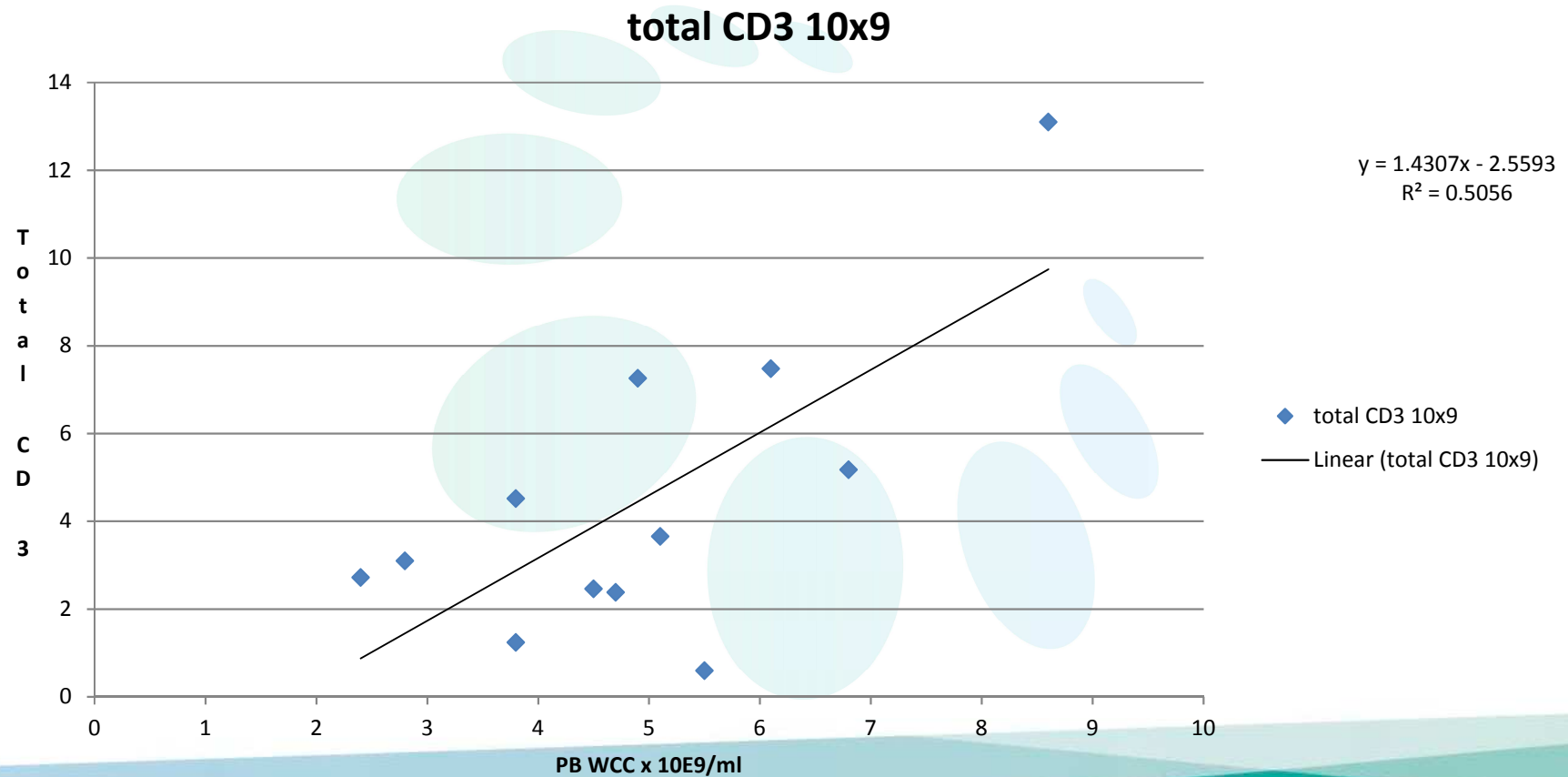
CD3+ Collection Efficiency



PB CD3 vs CD3 collected



PB WCC vs CD 3 collected



Summary

- cMNC significantly better than Optia MNC for collection efficiency ($p= 0.035$) and total CD3+ cells collected ($p= 0.011$)
- Target of $<2.5\%$ Hct met for all Spectra and 2/3 cMNC collections
- All Optia MNC collections had Hct $> 2.5\%$
- Granulocyte contamination lower with cMNC
- cMNC quicker and more predictable

Conclusions

- Optia cMNC was quicker, more efficient and more predictable with a higher TBV processed
- minimised non- target cell collection compared to Optia MNC
- Intermittent collection of Optia MNC led to less certainty around both collection volumes & procedure durations
- Staff acceptance of cMNC – more “intuitive”
- Optia cMNC is the platform of choice to replace the Cobe Spectra for steady state MNC collections for CAR - T cell and other novel therapies

Considerations for CAR-T leukapheresis

- Donors vs. patients
- Venous access – peripheral vs. central
- Yield vs. purity
- Man (woman) vs. machine
- Uniformity vs. individualised treatment
- Data, sharing, presenting and publishing!

Acknowledgements

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- Apheresis Unit - Jack Parrington; Claire Dowsing; Annette Favorolo
- CT Cryo & processing – Alannah Evans; Elise Ross; Carmen Chong; Ayse Mouminoglu
- Lori Boren
- Simon Harrison

Lunchtime tutorial – Friday 27th 1230hrs – Rm 335