SURVIVING THE EPO-CALYPSE

A Rising Cluster of Erythropoietin-associated Pure Red Cell Aplasia & Subsequent Response to Roxadustat - A Case Series

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JOHN'S STORY (2022)

68M, ESKD secondary to hypertension & atrophic left kidney

- Commenced PD, July 2021 → being worked up towards live donor transplantation from daughter

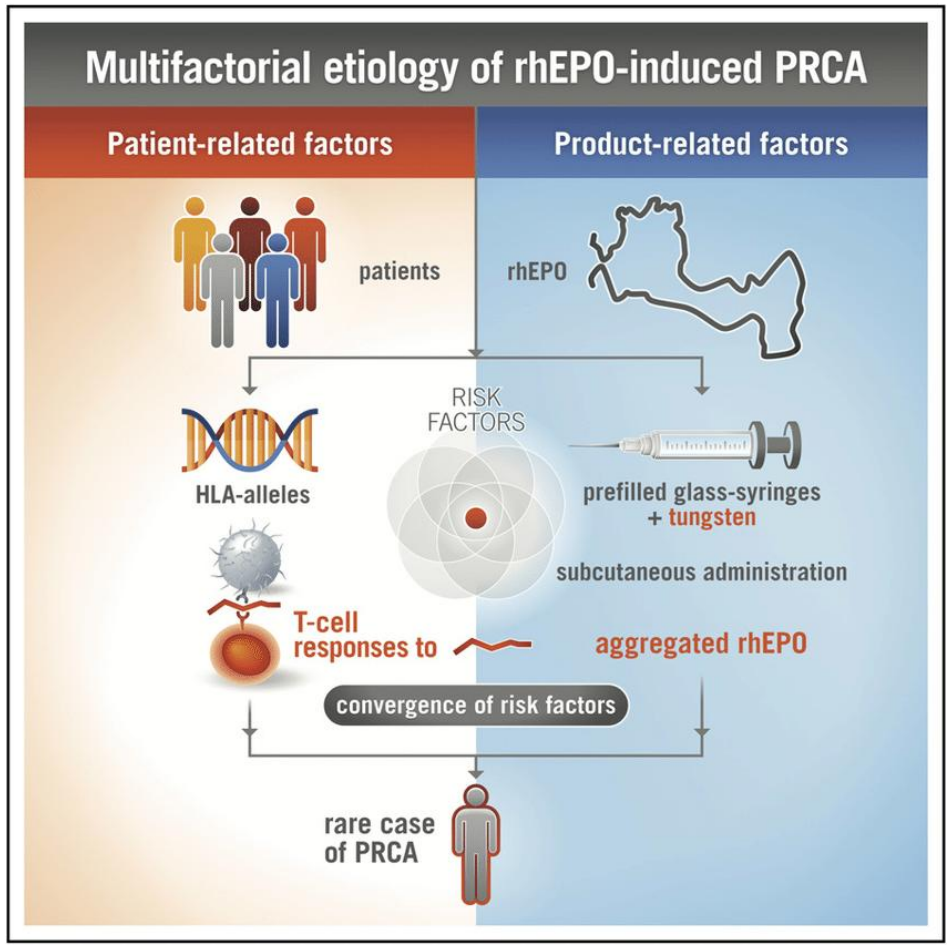
Sudden profound anaemia, Haemoglobin 58 g/L

- No cause found despite number of tests

5 months later: Anti-EPO antibody = positive, titre 4096

= diagnosis of ESA-PRCA

ESA-PURE RED CELL APLASIA



Profound anaemia with low reticulocytes and absent bone marrow erythroid precursors

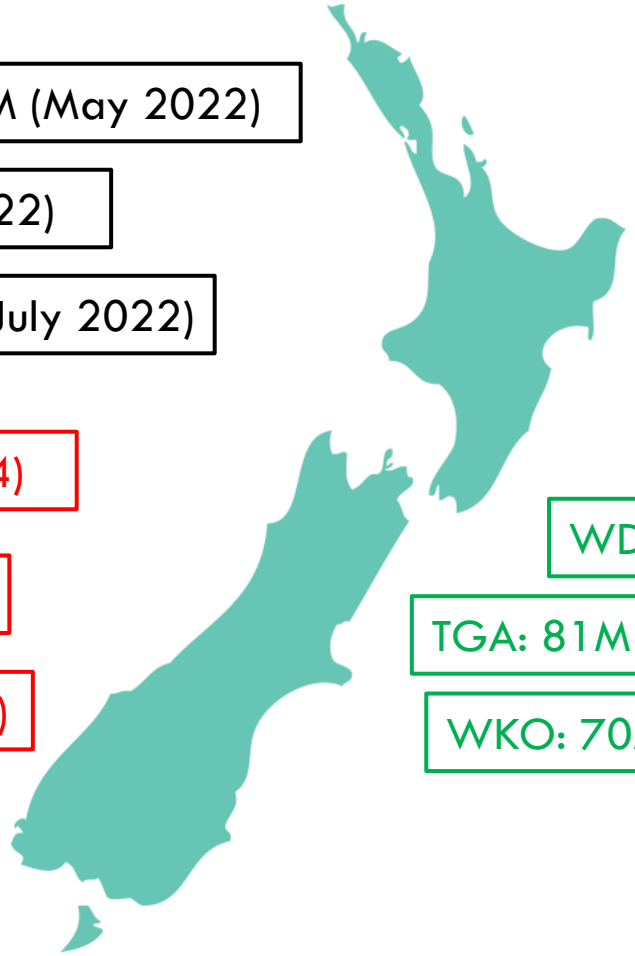
Described in patients treated with ESA

- Induction of neutralising antibodies
- "Very rare" → 1.6/10,000 patient years

Management

- Stop ESA (and all recombinant ESA products)
- Immunosuppression usually with ciclosporin, CYC, steroids, IVIG
- Optimal duration is unknown… probably continue until antibodies are undetectable?

SURPRISING (ALARMING) CLUSTERS OF NEW CASES!



2022

ADHB: 44M (May 2022)

CMDHB: 67M (May 2022)

WKO: 69M (July 2022)

2023

ADHB: 51F (May 2023)

ADHB: 46M (June 2023)

2024

WDHB: 79F (Nov 2024)

CMDHB: 68F (Nov 2024)

WKO: 61M (Nov 2024)

2025

WDHB: 68M (Jan 2025)

TGA: 81M (Jan 2025)

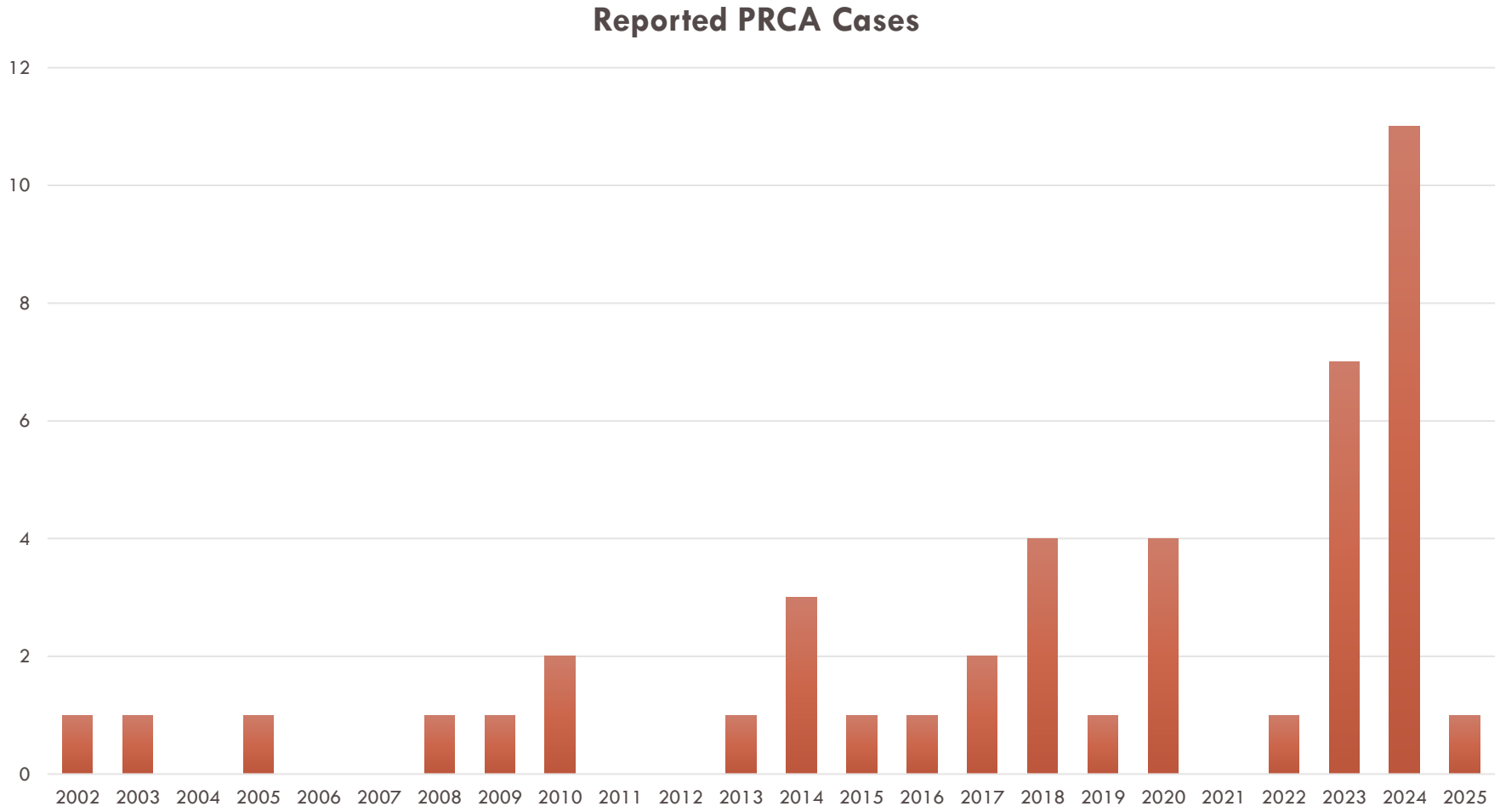
CMDHB: 57F (Feb 2025)

WKO: 70M (May 2025)

WDHB: 85M (May 2025)

*reliant on nephrology networking

44 CASES (2000-2025)



Median Age: 67.5
Mean Age: 63
Predominantly male (60%)
Median ESA (days): 214 (range 4-814)

**reliant on prescriber reporting*

OUR CASES (13): DEMOGRAPHICS

Median Age: 68 (range 44 – 85)

Mean Age: 65.2

Predominantly male (70%)

Median ESA duration (months): 10 (range 4-48)

Mean ESA duration (months): 13

Case	Date of Diagnosis	Age	Sex	Ethnicity	Cause of Kidney Failure	Stage of CKD	ESA Formulation & Administration	ESA (months)	Primary Diagnostic Method(s)
1	May 2022	44	M	Chinese	IgA Nephropathy	ESKD	Epoetin alfa, sc	9	BMB, positive antibodies
2	July 2022	69	M	NZ European	Hypertension	ESKD	Epoetin alfa, sc	8	BMB, positive (1:4096) antibodies
3	May 2023	51	F	Other European	ADPKD	ESKD	Epoetin alfa, sc	8	BMB
4	November 2024	61	M	NZ Maori	T1DM	CKD V	Epoetin alfa, sc	12	BMB, positive antibodies
5	May 2025	70	M	NZ European	Unknown	ESKD	Epoetin alfa, sc	7	BMB
6	June 2023	46	M	Southeast Asian	IgA Nephropathy	CKD IV	Epoetin alfa, sc	5	BMB
7	May 2022	67	M	NZ European	Hypertension	ESKD	Epoetin alfa, sc	4	BMB, positive (1:8192) antibodies
8	February 2025	57	F	Cook Island Maori	T2DM	ESKD	Epoetin alfa, sc	17	Declined BMB; consistent laboratory values
9	January 2025	81	M	NZ European	Hypertension	CKD V	Epoetin alfa, sc	10	BMB
10	November 2024	68	F	Samoan	T2DM	CKD V	Epoetin alfa, sc	13	BMB
11	November 2024	79	F	Other European	IgA Nephropathy	CKD V	Epoetin alfa, sc	12	BMB, positive antibodies
12	January 2025	68	M	Chinese	Hypertension	ESKD	Epoetin alfa, sc	48	BMB
13	May 2025	85	M	South Korean	T2DM	ESKD	Epoetin alfa, sc	17	BMB

OUR CASES (13): IMMUNOSUPPRESSION

Case	Nadir Hb (g/L)	RBC	Immunosuppression	Duration (months)	Disease/Treatment Complications
1	49	>30	Prednisone	10	Steroid induced diabetes
2	58	>30	Ciclosporin	13	Permanently delisted from transplant waitlist
3	51	>20	Prednisone, ciclosporin, tacrolimus	13	
4	44	20	Ciclosporin, prednisone	2.5	CSA/statin associated myopathy, commencement of dialysis, temporary deactivation from transplant waitlist
5	47	22	Ciclosporin	Ongoing	
6	60	10	Ciclosporin	3	
7	53	>30	Prednisone + cyclophosphamide, ciclosporin	2.5	Hypertension, hyperglycaemia
8	38	17	Prednisone, ciclosporin	Ongoing	
9	**59**	**12**	**Nil**	**N/A**	
10	48	13	Prednisone + cyclophosphamide	Ongoing	Hyperglycaemia
11	59	14	Prednisone	5	
12	**63**	**>50**	**Nil**	**N/A**	
13	56	28	Prednisone	Ongoing	

Predominantly monotherapy prednisone or ciclosporin (75%)

Two given dual (pred/CYC)

Four requiring immunosuppression switch

Seven completed immunosuppression → median duration: 5 months (range 2.5-13)

- No repeat antibody testing = 'best guess'

Two received no immunosuppression

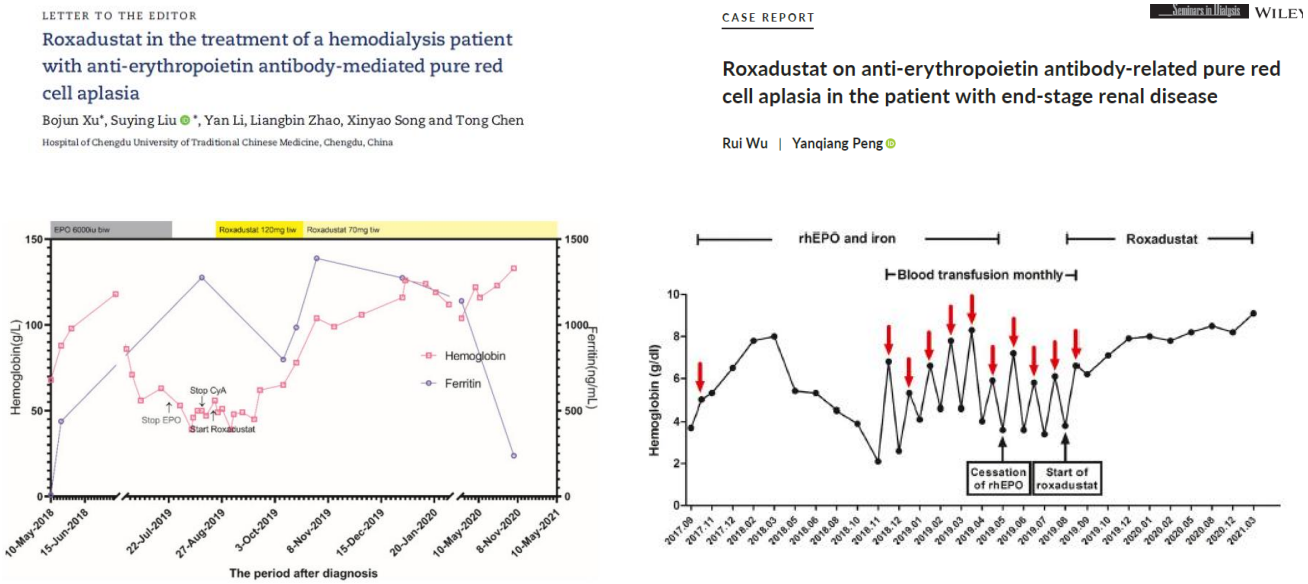
- Case 9: Frail/elderly
- Case 12: Significant comorbidities including cirrhotic liver disease, hepatitis B

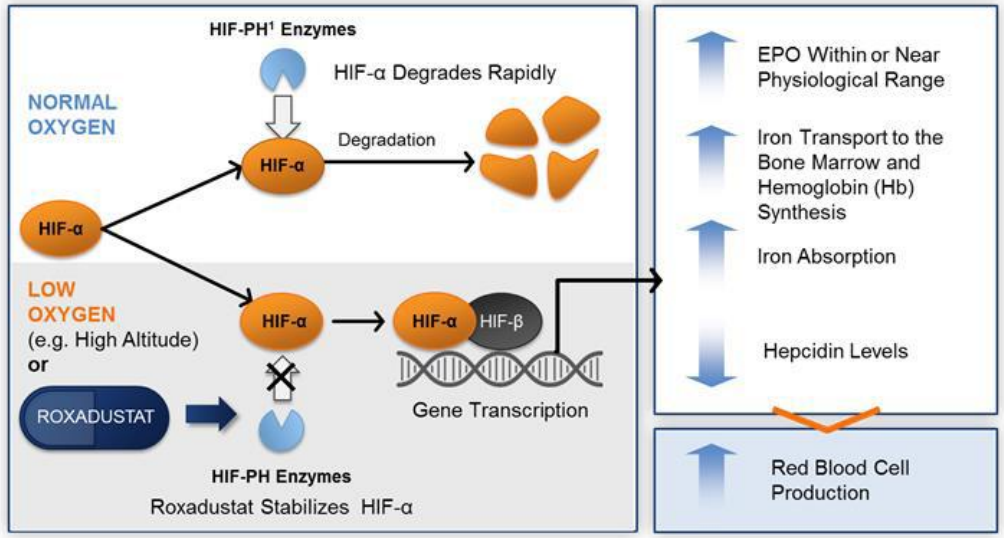
HIF* STABILISERS

= HIF-PHIs →Hypoxia-Inducible Factor-Prolyl Hydroxylase Inhibitors

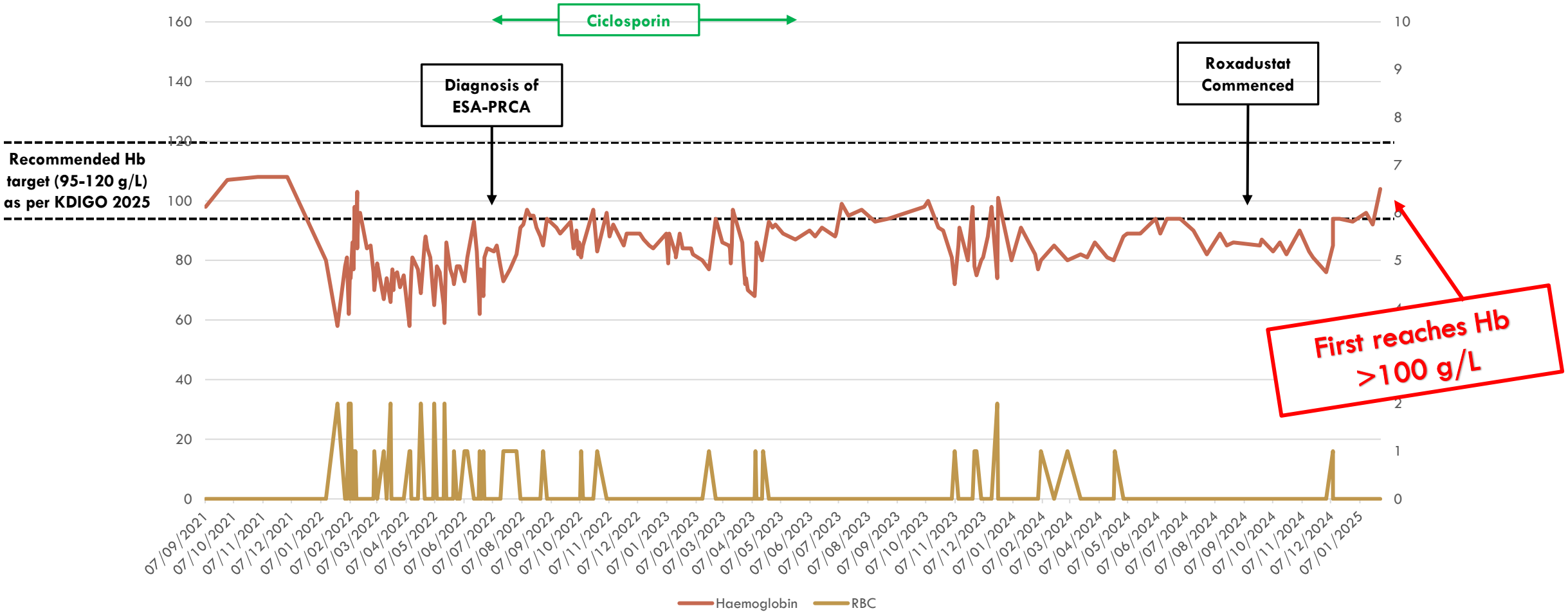
HIF = key regulator that controls how cells respond to hypoxic conditions

- Increases EPO synthesis, enhances iron uptake, opposes hepcidin





JOHN + ROXADUSTAT



OUR CASES (7/13): ROXADUSTAT

Case	PRCA Diagnosis	CKD Stage	Immunosuppression Commencement	Immunosuppression (months)	Roxadustat Commencement	Hb within target	Rox to target Hb (months)
1	May 2022	ESKD	July 2022	10	January 2024	April 2024	3
2	July 2022	ESKD	July 2022	13	October 2024	January 2025	3
4	November 2024	CKD V	November 2024	2.5	November 2024	March 2025	3
9	**January 2025**	**CKD V**	**N/A**	**N/A**	**February 2025**	**April 2025**	**2**
11	November 2024	CKD V	November 2024	5	February 2025	June 2025	4
12	**January 2025**	**ESKD**	**N/A**	**N/A**	**March 2025**	**Not reached**	**N/A**
13	May 2025	ESKD	July 2025	Ongoing	May 2025	Not reached	N/A

Seven patients commenced on Roxadustat → 5 reached target Hb (~3 months)

Six patients not commenced on Roxadustat → 1 reached target Hb (though CKD IV)

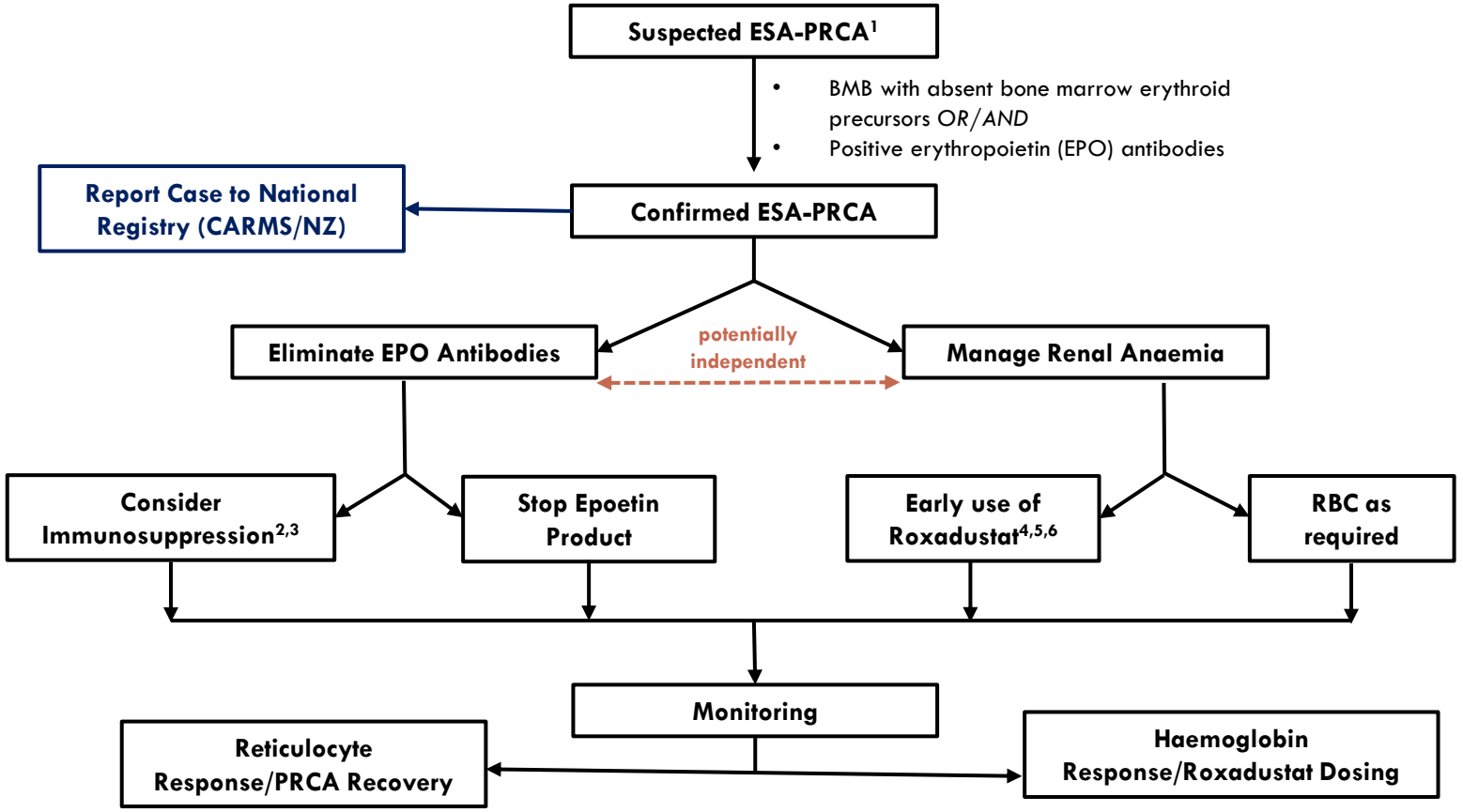
Two patients not commenced on Immunosuppression but received early Roxadustat

- One reached target Hb at 2 months
- Second commenced Roxadustat in March 2025 ?too soon to know

CONCLUSIONS & DISCUSSION POINTS

1. **Diagnostic Challenges**
   - Need high index of suspicion
   - Go for early BMB
   - **Importance of Reporting ADRs!**
2. **Treatment: Dual Pronged**
   - **Get rid of anti-EPO**
     - Stop Binocrit
     - Consider immunosuppression (no guidelines as to what/how long)
     - Consider NO immunosuppression if early Roxadustat/HIF-PHI is available
     - Use reticulocytes as a marker for recovery/remission (need to specifically ask for this to be checked each CBC)
   - **Manage Renal Anaemia**
     - Early use of Roxadustat – NPPA (in NZ) should be reasonably straightforward for similar cases
     - Consent/counsel patients around potential side effects

SUGGESTED MANAGEMENT ALGORITHM



[1]*Consider diagnosis of ESA-PRCA in patients treated with ESA who have refractory anaemia with reticulocytopenia*

[2]*Individualise immunosuppression using agent with lowest risk of adverse event for patient; aim for shortest duration using reticulocyte count to monitor recovery and remission*

[3]*Consider NOT using up-front immunosuppression if early Roxadustat is available, particularly in patients who have strong contraindications to immunosuppression*

[4]*Roxadusat used up to three times weekly, not on consecutive days, appropriate starting dose 70mg x3/week if <100kg; 100mg x3/week if >100kg; maximum dose 400mg x3/week*

[5]*Roxadustat $T_{1/2}$ 15 hours; not cleared with haemodialysis; 99% protein-bound*

[6]*Common adverse events with Roxadustat describe include hypertension, thrombotic vascular events; do not use in pregnant/breastfeeding patients, history of cancer or seizure*