Table 2: Candidate Chagas disease surrogate biomarkers. *Modified from the book Chagas disease, a clinical approach, Freilij, H., Altcheh, J., (Chapter Chagas Disease Treatment Efficacy Biomarkers: Myths and Realities, Ruiz-Lancheros et al.)*

Biomarker type	Biomarker	Results in Chagas disease	References
Parasite proteins	Trypomastigotes F2/3 antigenic fraction	Anti F2/3 decreases after BZN treatment and disappears after 4–21 months in children	120
	Immunofluorescence assay of fixed trypomastigotes (ISIFA)	High titers in infected patients and low titers 6 years after treatment when patients were considered cured. High sensitivity and no cross-reactivity with other diseases	112,162
	Trypomastigote mucin antigen A&T CL-ELISA	Measure anti-Gal Abs. Titers decrease after BZN treatment in adults and children	113,163,164
Parasite recombinant proteins	Ag13 85 kDa protein with repeats of 5 amino acids	Anti-Ag13 is suitable for CD diagnosis in different populations, and titers decrease and disappear after 3 years posttreatment	165
	T. cruzi ribosomal acid protein P2β	Levels of Anti-P2β decrease in asymptomatic treated CD patients	166
	Immunodominant antigens KMP11, HSP70, PFR2, Tgp63	A significant drop in reactivity against antigens between 6 and 9 months in BZN treated CD adults at different stages of the disease. Titers continue to drop after 24 months	167,168
	24 kDa calcium-binding protein (rTc24)	Anti-rTC24 Abs decreases within 6–36 months post-treatment	169,170
	Flagellar calcium-binding protein (F29)	Sero-reversion for the F29 antigen occurs between 6 and 48 months after BZN treatment in children	40,119
	Multiplex 16 r T. cruzi proteins	Decreased response of the panel 36 months after BZN treatment in adults	118,171
	Recombinant complement regulatory protein (rCRP)	Detect Abs complement-dependent as the CoML test. Positive reactions decrease 1–2 years after BZN treatment	172
	Putative microtubule-associated protein (MAP) antigen3	Selected antigen from a multiplex array of 15 antigens Results correlate with PCR-positive and PCR-negative results in a cohort study 5 years after BZN treatment	173
Host biochemical	ApoA1	Downregulated in CD and normal levels after BZN or NFX treatment	174,175

markers	ApoA1 and FBN fragments	Upregulated in CD and downregulated after BZN or NFX treatments	174,175
	Lytic antibody complement-mediated lysis (CoML) test	Abs decreases until becoming negative after parasite elimination in BZN and BFX treatments	170
Host prothrombotic markers	Prothrombin fragment 1 + 2 (F1 + 2)	A marker of thrombin generation in vivo increases early in CD and decreases after BZN treatment	176,177
	Endogenous thrombin potential (ETP)	Quantifies the ability to generate thrombin when activated through tissue factor addition upregulated in CD, decreases after BZN treatment	176,177
	Soluble platelet selectin (sP-selectin)	Biomarker of in vivo platelet activation decrease during BZN therapy in adults and children	177,178
Inmunological markers	IFN-γ T cells	Three-fold decrease compared with pretreatment between 1 and 3 years posttreatment	12
	CD3+ T cells	CD3+ T-cell proportion differs between treated and untreated patients and normalizes in cured patients	179
	IL12+ CD14+ cells	BZN-treated children show low levels of IL12+ CD14+ cells and high levels of IL-10 modulated type 1 cytokines profile	180
	CD4+ LIR+ T cells	Decrease of CD4+ LIR+ T cells after treatment between 2 and 6 months and for at least 2 years	47,181