BCL6-Positive Patients (Treated)

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BCL6 as a Marker of Uterine Lining Inflammation: A Retrospective Analysis of Treatment and Outcomes in Canada's Largest User

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BACKGROUND

BCL6 has been used since 2017 as a marker of uterine lining inflammation and strongly associated with endometriosis when overexpressed.[1] The positive predictive value of BCL6 among patients who underwent laparoscopy and were diagnosed with endometriosis was found to be 96% in independent studies.[6] Early prospective pivotal studies revealed that untreated BCL6-positive patients had significantly lower live birth rates on subsequent transfers compared to those who tested negative (LBR = 12% vs. 59%).[3] More recent prospective studies also showed similar results.[5] When these BCL6-positive patients were treated with a GnRH agonist or underwent laparoscopy, live birth rates significantly improved (52% treated vs. 12% untreated).[2] Since 2020, the largest user of the test in Canada has tested over 150 women, typically presenting with unexplained infertility (UI), recurrent implantation failure, or recurrent pregnancy loss. This retrospective cohort study is the first to demonstrate significant success rates from a Canadian fertility center among women testing positive and treated with Depot Lupron.

PURPOSE

To evaluate a subset of patients tested for BCL6 and treated with 60 days of Depot Lupron or Lupron with Letrozole and compare pregnancy and live birth success rates with previously published studies—adding to the clinical knowledge base of this protein marker, both generally and specifically within the Canadian infertility market.

MATERIAL & METHODS

150 patients were tested from 2020 to 2024. Patient history, lab results, and treatment data were reviewed. Patients whose outcomes were not yet available or who left the practice before completing treatment were excluded. BCL6-positive patients all received 60 days of a GnRH agonist or antagonist. Primary outcomes were pregnancy and live birth rates in the next subsequent transfer cycle. We examined subgroups based on patients tested for euploid embryos using PGT-A, failure history, and/or unexplained pregnancy loss (uRPL).

Inclusion Characteristics of Study Cohort Results

	Total (n=115)	BCL6 Positive (n=67)	BCL6 Negative (n=48)
PGT-A Tested	68%	64%	73%
Previous IVF Failure	70%	74%	65%
Average # of Failures	1.7		
uRPL	31%	36%	23%
Average Age	34.8		

RESULTS

BCL6-Positive Patients (Treated)

Treatment Modality	Patients	Pregnancy Rate	Live Births/Ongoing Pregnancies
BCL6 Positive (Total)	67	60 (90%)	46 (69%)
Lupron Depot (60 days)	31	29 (94%)	22 (71%)
Lupron + Letrozole 2.5 mg	33	29 (88%)	23 (69%)
Orilissa	3	2	1

BCL6-Negative Patients (Untreated)

Patients	Pregnancy Rate	Live Births/Ongoing Pregnancies
48	39 (81%)	28 (58%)

CONCLUSION

This patient cohort represents the challenging population of patients struggling to achieve pregnancy, even with genetically identified euploid embryos. Identifying and treating the subset of BCL6-positive patients with Depot Lupron or Lupron with Letrozole resulted in live birth rates far exceeding earlier prospective study outcomes (69% LBR vs 52% LBR, respectively),[2] and aligning with outcomes expected from first-time PGT-A tested IVF patients (72%).[5] In contrast, the BCL6-negative cohort had outcomes consistent with published success rates for a single embryo transfer in women without suspected uterine lining dysfunction.[2 3] This study provides continuing evidence of the efficacy of identifying and treating patients suspected of uterine lining inflammation, usually endometriosis, contributing to their infertility.

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