OUTCOMES IN WOMEN WITH IVF FAILURE WHO TESTED POSITIVE FOR BCL6 USING RECEPTIVADX™ TESTING: EFFECT OF TREATMENT ON SUBSEQUENT EMBRYO TRANSFER

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Background

Over the last 5 years, multiple studies have documented the value of BCL6 to predict IVF failure.[1-5] Many women presenting with unexplained infertility (UI) over-express the BCL6 oncogene, indicating inflammatory conditions including endometriosis. Endometrial biopsy combined with immunohistochemistry (IHC) for over-expression of BCL6, was shown to identify women with a significantly lower chance of a live birth compared to women who tested negative for this biomarker (LBR = 11% v 59%)[3]. However, when BCL6 positive subjects were treated for endometriosis with GnRH agonist suppression for 2 months or laparoscopy in controlled studies, LBR went up significantly compared to untreated controls (52% v 8%)[2]. While these published data are promising, the population included was relatively small. In an ongoing study, Cicero Diagnostics compiled and evaluated self-reported data from 7 IVF centers representing 189 women including 143 who tested positive and 46 who tested negative for BCL6 with subsequent embryo transfer and known outcomes over a 2-year period.

Objective

To establish ongoing treatment outcomes in women with positive ReceptivaDx results at multiple IVF centers compared to untreated BCL6 negative controls.

Materials and Methods

Three sources of data were used. First, information provided on the ReceptivaDx test requisition form including number of failed IFVs, other pre-existing conditions or previous diagnosis such as endometriosis, suspected hydrosalpinx, or PCOS. Second, the pathology results for BCL6 and third, the outcome data from the contributing centers. To minimize potential bias associated with unknown or missing prior history, we used live births including pending pregnancies with known treatment as our single end point. We only included patients treated with the recommended GnRH agonist (depot leuprolide acetate; Lupron®) or surgical laparoscopy. No information was available regarding prior PGS testing. These patients all presented with UI with 47% self-reporting at least one IVF failure.

Results

BCL6 Positive Patients Treated with GnRH agonist (Lupron) or Laparoscopy

	Patients Tested	Pregnancy Rates	Live Births and On-going pregnancies	Pregnant and Lost	Not Pregnant
BCL6 Positive	143	113 (79%)	92 (64%)	21 (15%)	30 (21%)
GnRHa*	103 (59%)	83 (81%)	70 (68%)	13 (13%)	20 (19%)
L/S*	40 (26%)	30 (75%)	22 (55%)	8 (20%)	10 (25%)

*Using Fisher's exact test, the P value equals 0.496 showing no statistical significance between GnRH and L/S as treatment choice.

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BCL6 Negative Patients Untreated

	Patients Tested	Pregnancy Rates	Live Births and On-going pregnancies	Pregnant and Lost	Not Pregnant
BCL6 Negative	46	31 (67%)	24 (52%)	7 (15%)	15 (33%)

Conclusions

The cumulative data from seven centers supports earlier published data on the value of BCL6 testing in women with UI undertaking IVF. In those studies, results showed positive BCL6 expression (histologic score, >1.4) was strongly associated with poor reproductive outcomes in IVF cycles in women with UI and a blended 51% LBR after treatment [2,3.] Our self-reported outcomes data is slightly higher at 64% with the caveat that not all pregnancies were complete at time of submission. Negative BCL6 results predicted favorable outcomes (67% pregnancy rate) consistent with the 65% pregnancy rate in previous studies[3].

Positive BCL6 results treated with either laparoscopy or GnRH agonist showed improved outcomes (79% pregnancy rate and 64% LBR or on-going pregnancies). BCL6 positive patients treated with Lupron showed the highest pregnancy rates (81%) and live birth/on-going pregnancy (68%) rates. Because this study was a compilation of self-reported data, more prospective randomized studies are needed to definitively prove the value of both testing and treatment of affected women. A current NIH grant awarded Cicero Diagnostics and currently in the second phase will attempt to replicate the findings shown here and in the published papers. Phase II will cross multiple centers including Wake Forest, Stanford, and University of North Carolina.

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References:

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