UCBG 2-14: A prospective multicenter non-randomized trial evaluating the effect of EndoPredict® (EPclin®) clinico-genomic test on treatment decision making among patients with intermediate clinical risk

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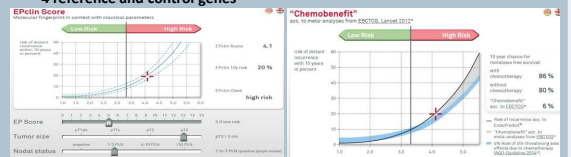
Background & Objective

Genomic tests can identify ER-positive Her2-negative localized breast cancer (BC) patients (pts) who may not drive any benefit from adjuvant chemotherapy (CT). Several genomic tests have reached a high level of analytical and clinical validity, as well as clinical utility in such situation. Recent results suggest that the safe de–escalation of adjuvant chemotherapy may be most beneficial in pts with clinical high or intermediate risk, as assessed by classical variables or online tools, through the use of a genomic test. The clinical risk though remains quite uncertain with variable definition and grey zones.

EndoPredict® is a multi-gene test for breast cancer patients. The test consists of a molecular finger print determined by the gene expression within the tumor tissue and is combined with the clinical status of the tumor. It includes:

- 3 proliferation-associated genes
- 5 hormone receptor-associated genes
- 4 reference and control genes



The present study aimed at determining if EPclin® clinico-genomic test had a significant impact on treatment decision making among pts with predefined intermediate /borderline clinical risk.

Objectives

Primary objective: To assess EPclin® genomic test clinical utility defined as impact on chemotherapy decision in the adjuvant setting in patients with ER-positive, Her2-negative early breast cancer with uncertainty on the indication of chemotherapy using standard assessments.

Secondary objectives are PROs (Patient Reported Outcome) and descriptive analyses

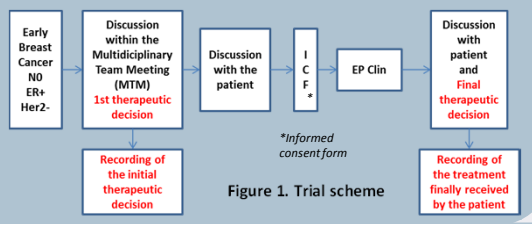


Figure 1. Trial scheme

Patients and Methods

- Between Dec 2015 and May 2016, 203 patients were enrolled. (Data available for 201 patients at the time of the analysis).

Women were eligible for the present study if they:

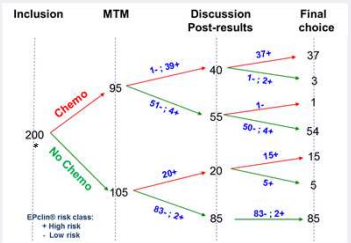
- had an histologically confirmed, invasive breast cancer
- had complete surgical removal of a localized ER+ Her2- pN0 or pN1mi BC,
- were considered by the multidisciplinary team meeting (MTM) of the center as being in a "grey zone" of uncertain CT benefit based on classical clinic-pathological assessment, outlined in the following situations:
  - Lobular histology
  - Or grade II
  - Or grade III and pT < 2cm

Description of the Patients Population

		N	Result
Median age	years	201	57.5 +/- 10 (27.2-81)
Tumor Type	Ductal Lobular Other		72% 15% 13%
Multiple Foci	Yes		12%
Tumor Grade	I II III	17 149 35	9% 74% 17%
ER+		201	100%
PR+		166	82.5%
Surgery	Lumpectomy Mastectomy	149 52	74% 26%
	Sentinel Node		89%
pT	pT1 pT2 pT3	151 44 5	75.5% 22% 2.5%
pN	pN0 pN1	181 19	90.5% 9.5%
EPclin® risk class	Low risk High risk		67% 33%

Results

Evolution of therapeutic strategy according to MTM and EPclin® classification

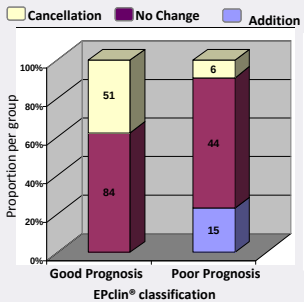


*1 patient excluded from analysis because of metastasis discovery after inclusion

The overall change rate of chemo decision is 72/200 (35.8% CI-95% = [29.2-42.4]).
In 57 cases, chemotherapy was withdrawn (28.4% [22.2-34.8])
In 15 cases (7.5% [3.8-11.2]) chemotherapy was added.

This rate is strictly in line with expectations (30% to 40%), and, since the confidence interval does not include 15%, a threshold below which the test would not be considered interesting, we can conclude that the EndoPredict® test is useful in the conditions of this trial.

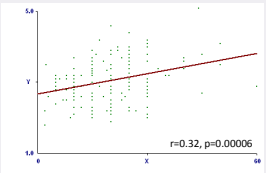
Reasons for change: The EPclin® classification is the essential reason for a change in therapeutic strategy



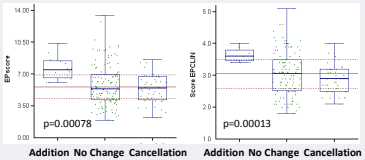
	Treatment changes toward chemo N (%)		
EPclin® risk class	Addition	No change	Removal
Good Prognosis	0 (0.0%)	84 (62.2%)	51 (37.8%)
Poor Prognosis	15 (23.1%)	44 (67.7%)	6 (9.2%)
Total	15	128	57
	EP-risk* per group (Mean [Range])		
Good Prognosis	-	6 [2-10]	6 [3-10]
Poor Prognosis	13 [10-18]	17 [10-45]	14 [11-19]

* Risk of distant recurrence at 10 years

Significant correlation between Ki67 and EPclin®



EPscore (molecular) is slightly less discriminating for changes in therapeutic decision than the EPclin® (composite) score.



Patient-reported outcome Results

p value results are indicated

Situation regarding chemo	Satisfaction (IN-PATSAT32)	Distress	State Anxiety
Decision change	0.59	0.94	0.018 Change= ↗
Addition/no change/cancellation	0.61	$< 10^{-7}$ addition= ↗	$< 10^{-7}$ Addition= ↗
Initially planned	0.47	0.19	0.54
Finally decided	0.37	10^{-6} chemo = ↗	0.012 chemo = ↗

No significant impact of the "procedure" on the evolution of patient satisfaction, but significant, albeit variable, impacts on distress and anxiety-state.

Conclusions

- Adendom met its primary objective: A very significant chemo decision change rate between primary decision and final administration, was observed = 35.8% of which 7.5% in favor of an addition of chemo and 28.4% of its withdrawal.
- The changes essentially contradict the prognostic meaning of SBR grade and KI-67.
- One third of the "grey zone" patients had high risk EPclin® score.
- Treatment decisions and change levels were heterogenous across centers (not shown).
- Satisfaction was high, but delayed chemotherapy decision and changes towards addition of chemo were associated with high distress levels.

Acknowledgments

Patients

CENTRE JEAN PERRIN - CLERMONT-FERRAND; INSTITUT GUSTAVE ROUSSY – VILLEJUIF; INSTITUT SAINTE CATHERINE – AVIGNON; CENTRE FRANCOIS BACLESSE – CAEN; CENTRE HENRI BECQUEREL – ROUEN; INSTITUT DE CANCEROLOGIE DE LORRAINE ALEXIS VAUTRIN - VANDOEUVRE-LES-NANCY; HOPITAL PRIVE JEAN MERMOZ - LYON CENTRE HOSPITALIER DE CORNOUAILLE – QUIMPER; INSTITUT DE CANCEROLOGIE LUCIEN NEUWIRTH; INSTITUT BERGONIE – BORDEAUX; INSTITUT JEAN GODINOT – REIMS; CLINIQUE CLAIRVAL – MARSEILLE; CHD VENDEE - LA ROCHE SUR YON; CENTRE HOSPITALIER DE LA DRACENIE - DRAGUIGNAN; CENTRE CATHERINE DE SIENNE - NANTES CENTRE HOSPITALIER DE PAU; CLINIQUE SAINT PIERRE – PERPIGNAN; CENTRE HOSPITALIER DE CHOLET - CHOLET CLINIQUE CHENIEUX – LIMOGES; CENTRE HOSPITALIER SAINT JEAN – PERPIGNAN; CENTRE AZUREEN DE CANCEROLOGIE – MOUGINS; CENTRE EUGENE MARQUIS – RENNES; HOPITAL LOUIS PASTEUR - CHARTRES - LE COUDRAY; CENTRE HOSPITALIER UNIVERSITAIRE – LIMOGES; CLINIQUE SAINT JEAN DU LANGUEDOC - TOULOUSE

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