*Webinar:* **Genomic Profiling and the Future of Early Breast Cancer Care.**

# Real-world and health-economic evidence supporting Prosigna adoption for routine management of adjuvant therapy

Roman ROUZIER, MD, PhD

Department of Surgery

Institute Curie - Hospital Network - Saint-Cloud, Paris

institutCurie

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# Mrs BM

- 68 years old
- **Mammograms 6/06/20:** ACR5
  - 22 mm mass in the breast. Normal left axillary ultrasound. Biopsy: IDC
- Surgery: lumpectomy and lymph node biospy
- Pathology:  IDC grade II 28 mm, LVE +
  - 2 Sentinel Nodes negative
  - ER+, PR+, Ki67 12%
- Quite large tumour but quite favourable biology
- Chemotherapy ?

# Mrs BM

- 68 years old
- Pathology:  IDC grade II 28 mm, LVE +,
  - 2 Sentinel Nodes negative,
  - ER+, PR+, Ki67 12%
- Chemotherapy?
- **Prosigna:**
  - Luminal A
  - ROR: 38
  - Probability of recurrence: 7%, low risk

# Mrs MT

- 54 years old
- **Mammograms 12/06/20: ACR5**
  - 7 mm mass in the breast. Normal left axillary ultrasound. Biopsy: IDC.
- Surgery: lumpectomy and lymph node biospy
- Pathology:  IDC grade III 12 + 5 + 2 mm, LVE +
  - N0(i+) ,
  - ER+, PR-, Ki67 40%
- Quite small tumor but multifocal but unfavorable biology
- Chemotherapy ?

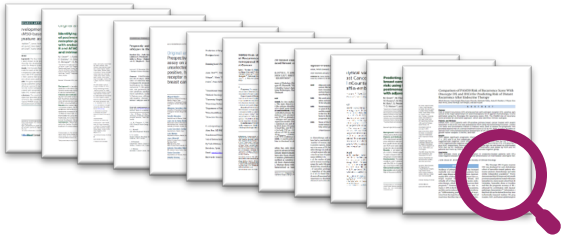
# Mrs MT

- 54 years old
- Surgery: lumpectomy and lymph node biospy
- Pathology:  IDC grade III 12 + 5 + 2 mm, LVE +
  - N0(i+), ER+, PR-, Ki67 40%
- Chemotherapy ?
- **Prosigna:**
  - Luminal B
  - ROR: 78
  - Probability of recurrence: 28%, high risk

# 2 Classical Cases

- Additional information
- Improve confidence in treatment choice
- Evidence ?
- Real-world at the level of a population: how many tests to avoid chemo in one patient
- Cost-effectiveness ?

# Prosigna's Evidence Base



**TransATAC (n = 1,007)**
- 10y DR: Dowsett et. al. *JCO* 2013
- Late Recurrence: Sestak et. al. *JNCI* 2013
- Six Algorithm Comparison: Sestak et. al. *JAMA Onc 2018*

**ABCSG.8* (n = 1,478)**
- 10yr DR: Gnant et al. *Ann Onc* 2013
- Late Recurrence: Filipits et. al. *CCR* 2014
- Local Recurrence: Fitzal et al. *ASCO* 2014

**Combined Analysis (n = 2,485)**
- Node Positive: Gnant et al. Ann Onc 2015
- Late Recurrence: Sestak et. al. JCO 2015

**DBCG Population-based Cohort Study (n = 2,558)**
- 10yr DR: Lænkholm et al. *JCO 2018*
- Node Positive: Ejlertsen et al. *ASCO* 2015
- Late Recurrence: Lænkholm et al. *ASCO* 2015
- Local Recurrence: Eriksen et al. *SABCS* 2015
- Special Subtypes of BC: Lænkholm et al. *Acta Oncologica* 2018

**Relative Effect of Chemotherapy by Risk Group**
- Multi-Center Spanish Cohort: Prat et al. *Clin Can Res* 2016
- Danish Randomized Study DBCG77B: Jensen et al. *Breast Cancer Research* 2018
- Danish Randomized Study DBCG89D: Jensen et al. npj Breast Cancer 2020
- Candian MA.5 Study: Cheaung M et al. Clinical Cancer Research 2012

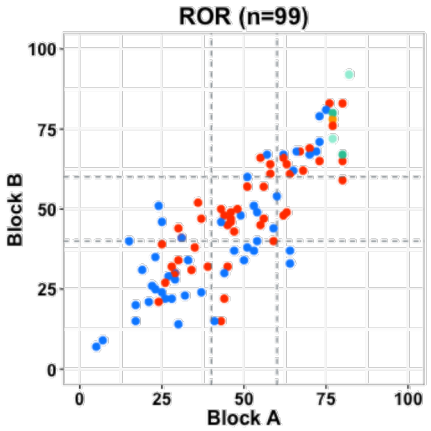
**Decision Impact Studies (n = 600)**
- Spain: Martin et al. *Curr Med Res Opin* 2015
- Germany: Wuerstlein et al. *Curr Med Res Opin* 2016
- France : Hequet et al. PLOSOne 2017

**Prognostic significance across histological subtypes**
- Special Subtypes: Laenkholm AV *Act Oncologica 2018*
- Lobular and Ductal Carcinoma: Laenkholm AV *Clinical Breast Cancer 2020*

# Evidence for Prosigna

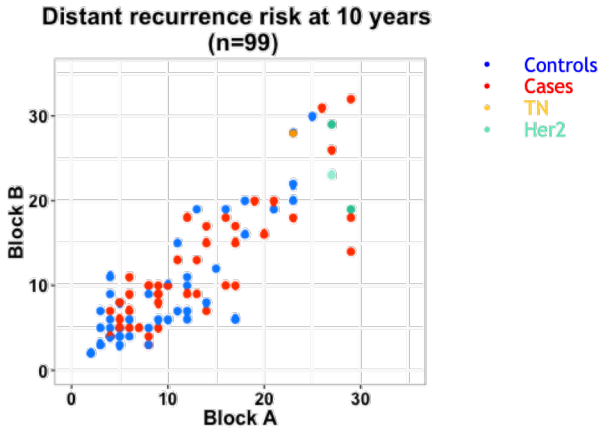
- The test is robust and provides additional information to IHC (28% of discordance)
- Other Questions:
  - Clinical utility beyond decision impact studies?
  - Real-world and health-economic evidence?

## ROR score and recurrence risk are highly correlated between different blocks of the same tumor




Pearson : R = 0,84 (p< 2.2e-16)

Cases: p=9.148e-14
Controls: p=7.239e-14




Pearson : R = 0,86 (p<2.2e-16)

Cases: p=1.665e-14
Controls: p< 2.2e-16

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# Concordance clinical-biological subtypes vs Prosigna subtypes – Decision Impact study

| | | Subtype by Prosigna test results | | | | |
|---|---|---|---|---|---|---|
| | | Lum A | Lum B | HER2-E | Basal | TOTAL |
| Suntype by IHC | Lum A | 94 | 31 | 1 | 0 | 126 |
| | Lum B | 20 | 48 | 0 | 2 | 70 |
| | HER2-E | 0 | 0 | 0 | 0 | 0 |
| | Basal | 0 | 0 | 0 | 0 | 0 |
| | TOTAL | 114 | 79 | 1 | 2 | 196 |
| Concordance | | 75% | 69% | NA | NA | 72% |

**TAKE HOME MESSAGE : 28% discordance**

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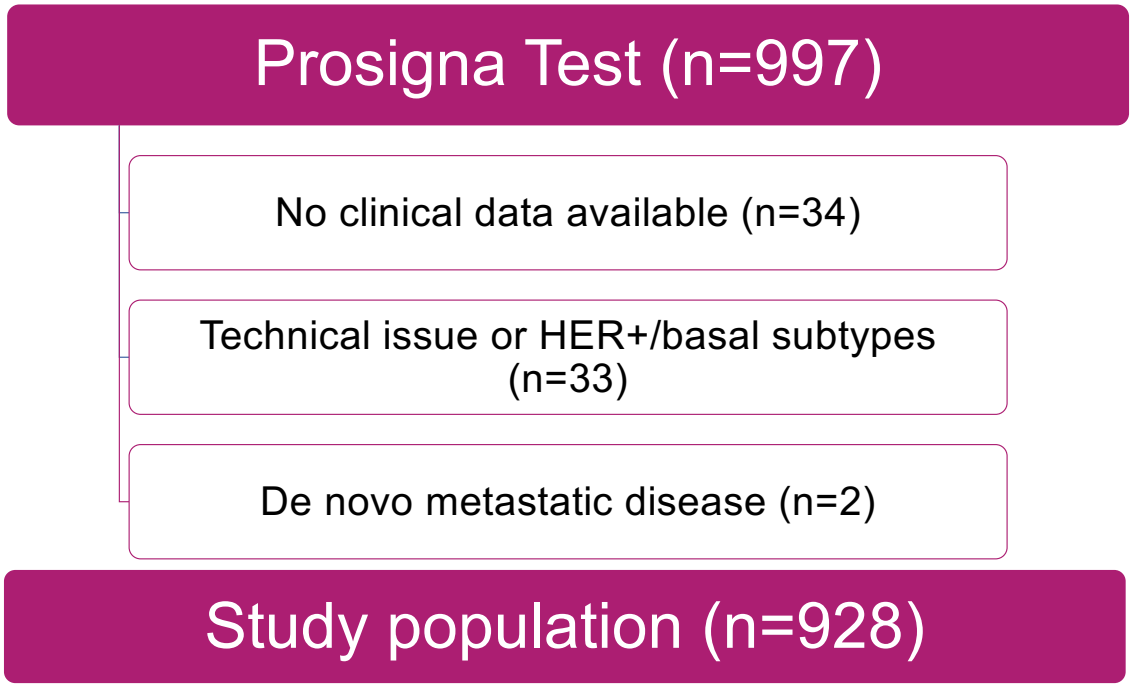
# Real-world patients = prospective, selection, real impact

- Cohort study on genomic tests usage for HR+, HER2- early breast cancer patients
- Single comprehensive cancer center
- Real-life setting, from January 2016 and December 2020.
- Data were collected prospectively and included:
  - age
  - tumour characteristics
  - Prosigna tests results
  - treatments administered
  - follow-up
- Sensitivity analysis

# Indication of Prosigna test

- Genomic tests to help adjuvant chemotherapy decision were performed for HR+, HER2-, >pT1b breast cancer patients with intermediate risk of recurrence, defined by:
  - Grade 1 tumours: pT1cN1 OR pT2N0/N1
  - Grade 2 tumours: pT1cN0/N1mic with Ki67>20 and/or Lympho-vascular emboli (LVE) OR pT2N0/N1mic
  - Grade 3 tumours: pT1cN0
- Health authorities guidelines in 2019: pT1c-2 N0-1mic and grade 2 tumours

# Real-world patients = prospective, selection, real impact

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# Patients Characteristics

- All these patients were candidate for chemotherapy before using the genomic tests.
- Indication of chemotherapy according to Prosigna test results:
  - 10-years metastatic risk of recurrence > 10% in post-menopausal patients
  - > 10% 7% in pre-menopausal patients

| | n/mean | %/range |
|---|---|---|
| Age (years) | 57 | (26-83) |
| Size (mm) | 20 | (3-80) |
| GRADE | | |
| 1 | 87 | 9% |
| 2 | 709 | 76% |
| 3 | 132 | 14% |
| Lymphovascular emboli (LVE) | | |
| No | 747 | 80% |
| Yes | 181 | 20% |
| LYMPH NODE INVOLVEMENT | | |
| pN0 | 737 | 79% |
| pN1mic | 89 | 10% |
| pN1 | 102 | 11% |
| Ki67 | 20 | (0-100) |

# Costs

- Based on data obtained from a previous prospective study on a similar early breast cancer population.
- Additional cost of chemotherapy over a year:
  - direct medical (medical consultation, treatments, hospitalization, imaging…) and non-medical (medical leaves, transportation…)
  - Estimation: 9737 €
- Cost of the Prosigna genomic test as defined by the reimbursement system was 1849€.
- Both costs are at a National Health Insurance perspective.

# Results of the Prosigna assay

- Chemotherapy was not indicated by the Prosigna test for 405 patients, giving a 44% decrease in chemotherapy indications.

- To avoid adjuvant chemotherapy for one patient, 2.3 Prosigna tests had to be performed in our whole population.

| | n/mean | %/range |
|---|---|---|
| **SUBTYPE** | | |
| Luminal A | 505 | 54% |
| Luminal B | 423 | 46% |
| **CONTINUOUS RISK** | | |
| ROR score | 47 | (0-93) |
| 10y risk of distant recurrence | 13 | (2-48) |
| **RISK CATEGORY** | | |
| Low | 251 | 27% |
| Intermediate | 371 | 40% |
| High | 306 | 33% |

# Medico-economic impact

1849,5€
x 928

928 tests performed
= 1 716 336 €

405 chemo avoided
= 3 943 485 €

9737€
x 405

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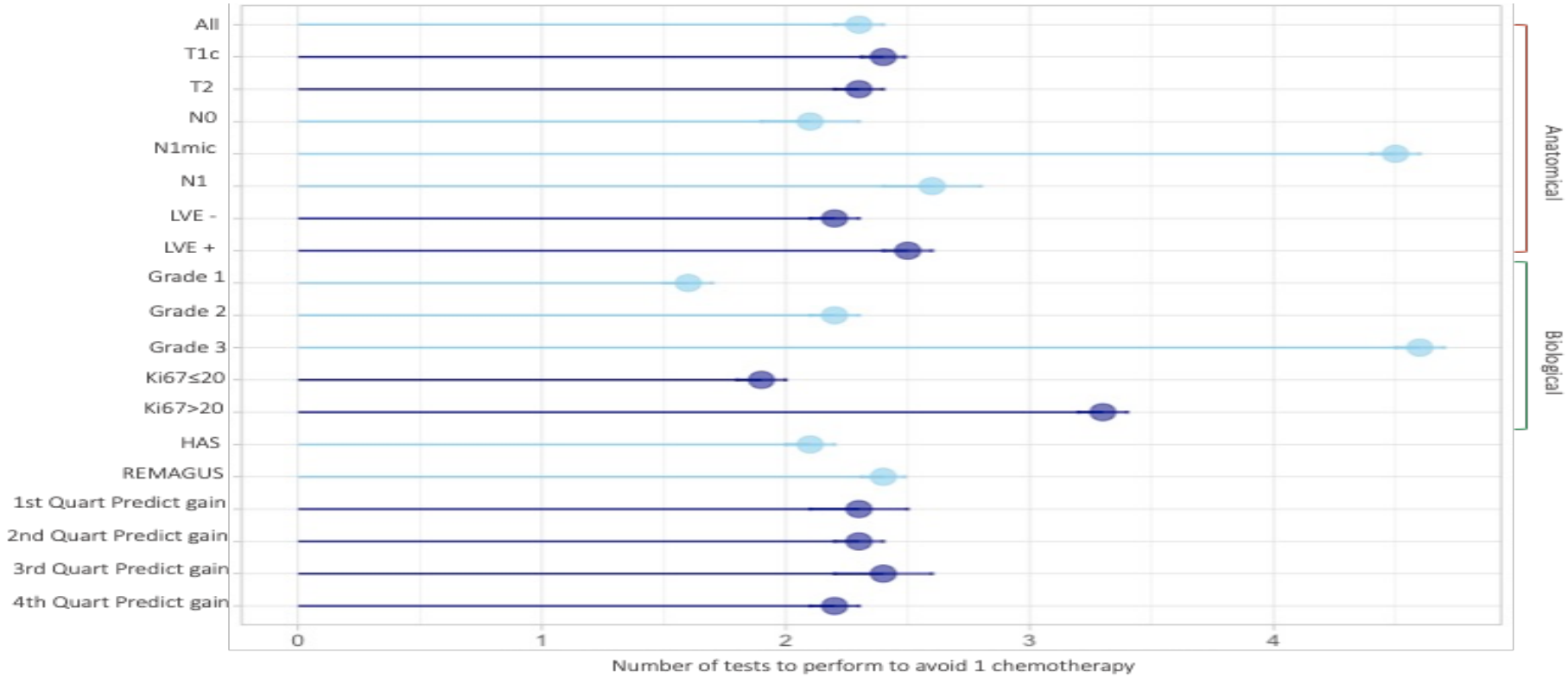
# Avoidance of Chemotherapy

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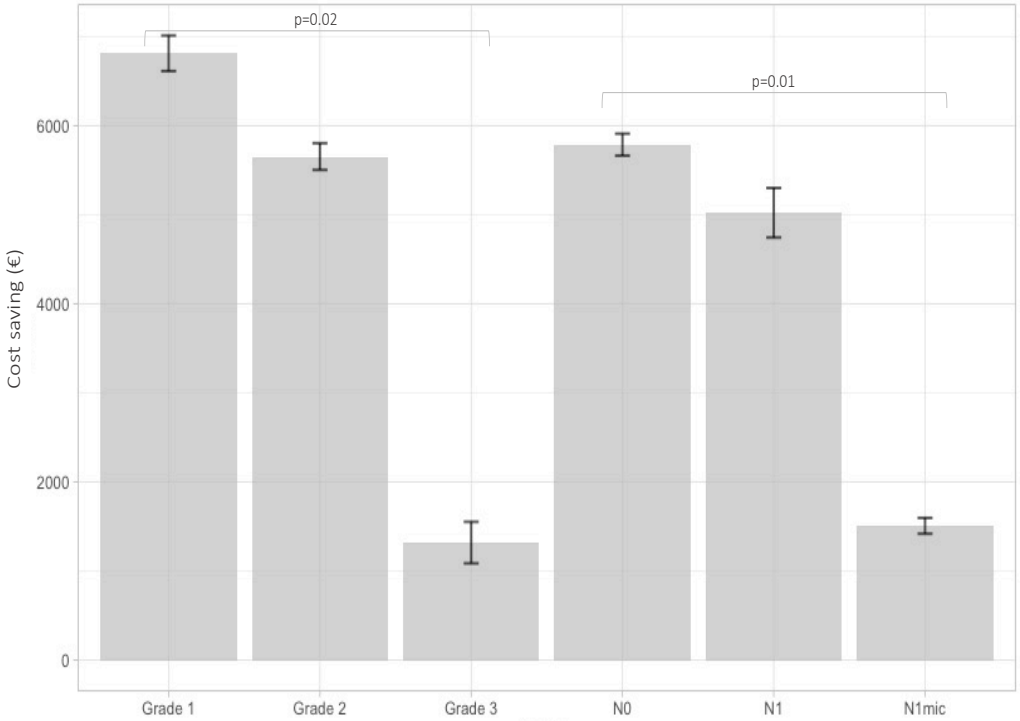
# Medico-economic impact

- 2.3 tests (cost of a Prosigna test: 1849€) to avoid chemotherapy for 1 patient (extra cost of chemotherapy: 9737€)
- the costs saved when performing Prosigna tests to avoid one adjuvant chemotherapy were 5299 € (2400€/patient).
- Cost-saving strategy !

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# Cost-effectiveness Vs Cost-savings

- Cost-effective is different from cost-saving!
- Cost-effective: improvement in health outcome for a “reasonable” increase in cost / “good value for money”
- Cost-savings: improvement in health outcomes and saving in total costs

**Very few healthcare innovations are cost-saving…**

**Prosigna is !**

## Question 1 From Registered Participant For Dr. Rouzier:

# What is the clinical relevance of the intrinsic subtypes identified by PAM50 and why are they different than IHC-identified subtypes?

## Question 2 From Registered Participant For Dr. Rouzier:

# What is the most important patient population to determine gene signature in clinical practice for early BC?