

Residual disease after neoadjuvant therapies

Introduction

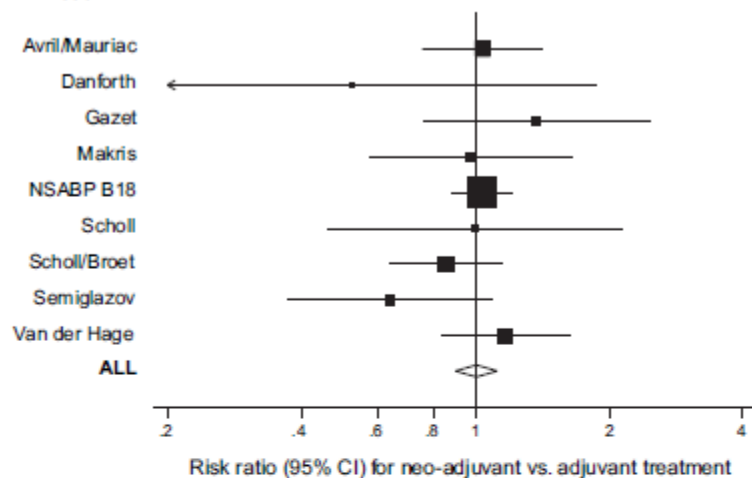
Suzette Delaloge, MD

Institut Gustave Roussy, Villejuif, France

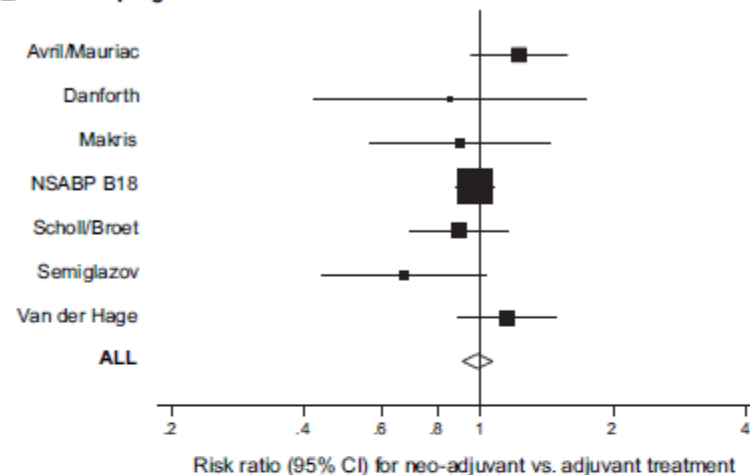
Neoadjuvant therapies for early BC: where do we stand?

- Neoadjuvant = adjuvant / survival in the overall population
- Up to now, individual patients' benefit = conservation only

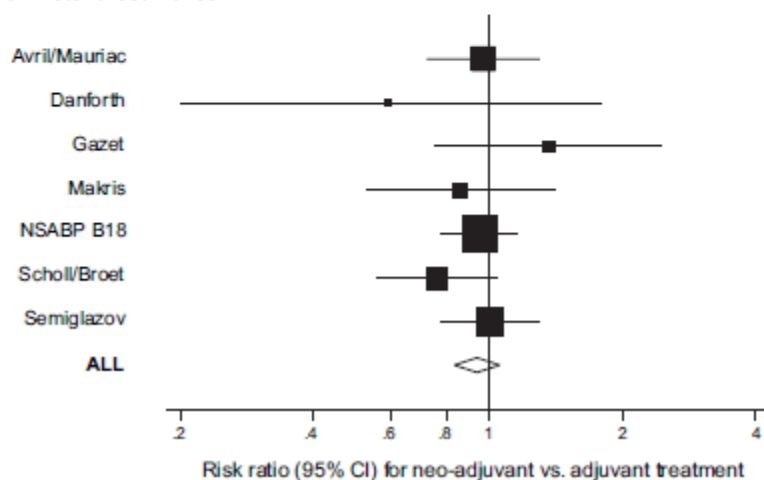
A Death



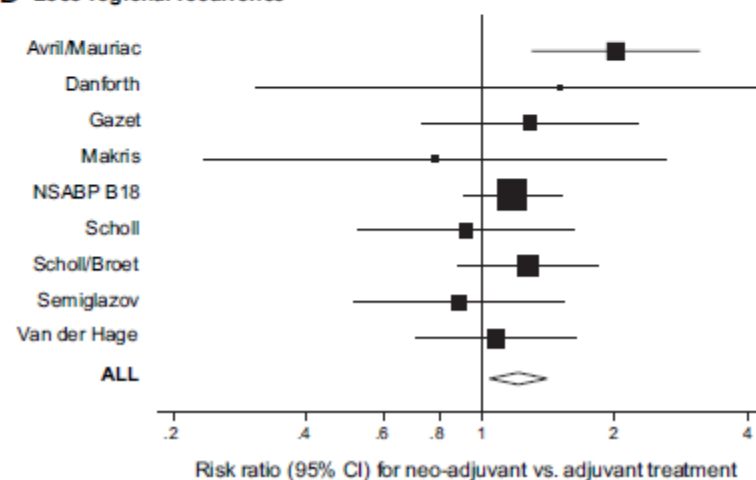
B Disease progression



C Distant recurrence



D Loco-regional recurrence



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- pCR is not a surrogate end-point for survival in the overall population

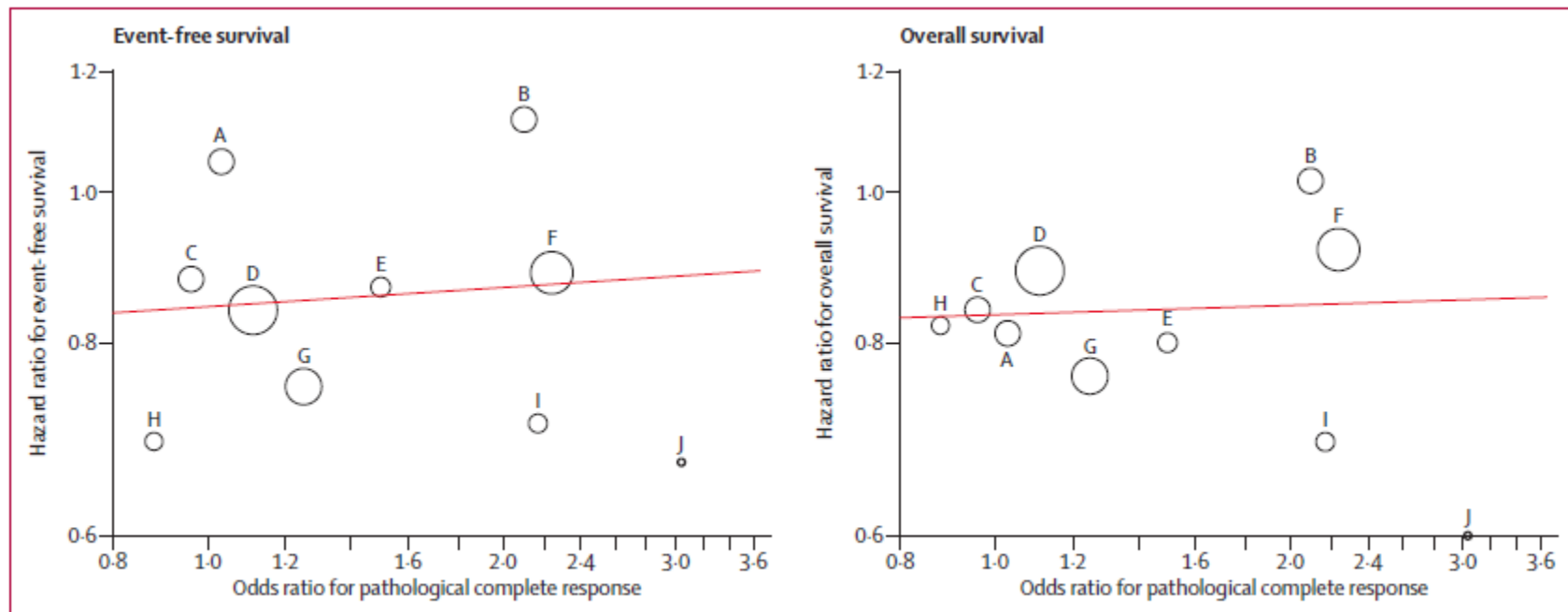
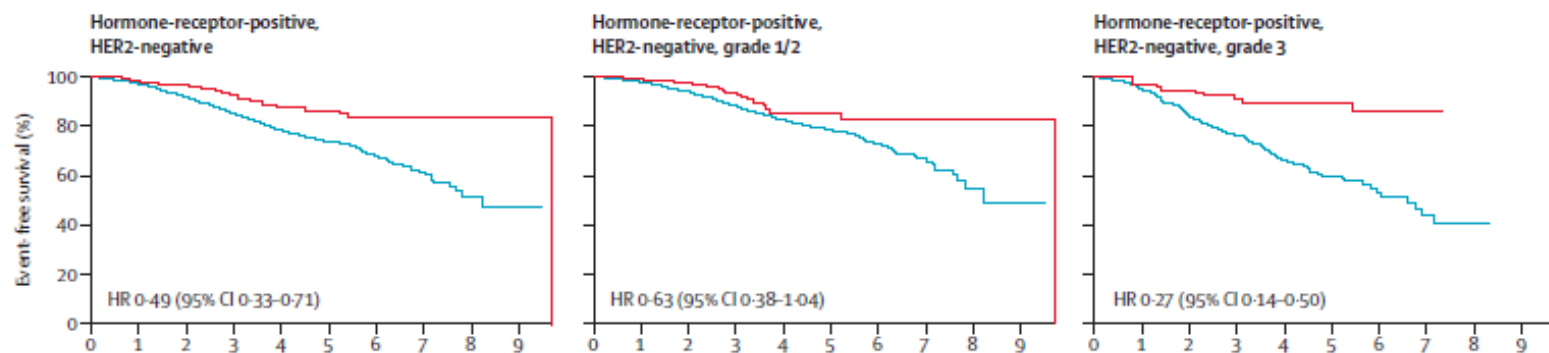


Figure 6: Trial-level correlation between treatment effect on pathological complete response and event-free survival or overall survival

Cortazar et al Lancet 2014

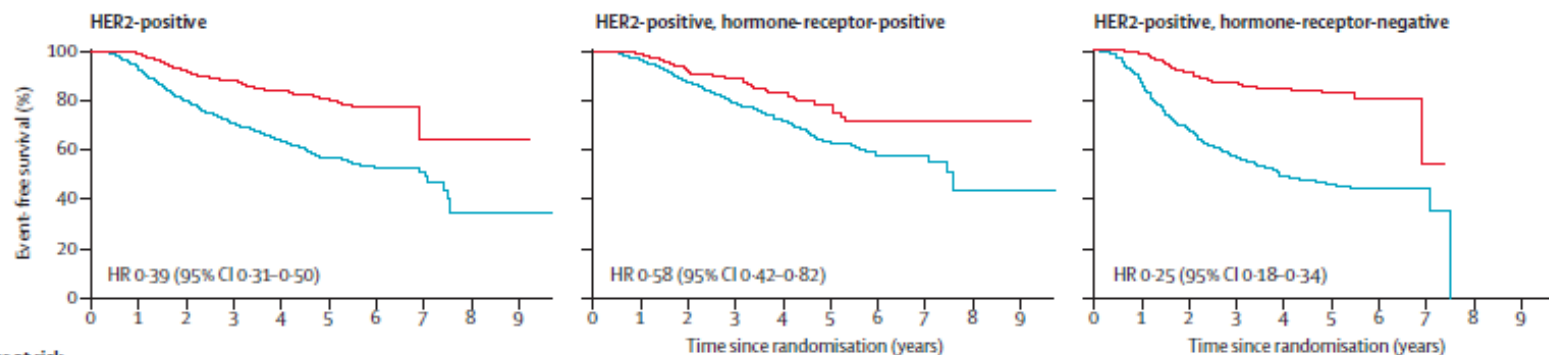
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- pCR is not a surrogate end-point for survival in the overall population
- Response-driven treatment still investigational
- Residual disease (breast/LN) is negatively associated with prognosis in most subtypes → can serve as predictor of relapse despite optimal treatment... **PRONOSTIC VALUE**



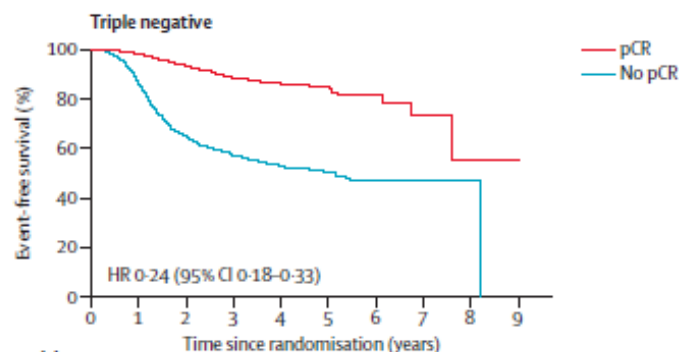
Number at risk

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--------|------|------|------|------|------|-----|-----|----|----|---|------|------|------|------|-----|-----|-----|----|----|---|-----|-----|-----|-----|-----|-----|----|----|---|
| pCR | 270 | 244 | 224 | 184 | 113 | 69 | 21 | 6 | 2 | 2 | 148 | 134 | 123 | 102 | 55 | 33 | 10 | 5 | 2 | 2 | 102 | 92 | 83 | 71 | 49 | 30 | 9 | 1 | 0 |
| No pCR | 2491 | 2226 | 1978 | 1616 | 1017 | 658 | 247 | 84 | 20 | 1 | 1838 | 1653 | 1493 | 1236 | 790 | 517 | 198 | 68 | 15 | 1 | 528 | 458 | 376 | 290 | 173 | 111 | 38 | 14 | 5 |



Number at risk

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--------|------|------|-----|-----|-----|-----|-----|----|---|---|-----|-----|-----|-----|-----|-----|----|----|---|---|-----|-----|-----|-----|-----|----|----|---|
| pCR | 586 | 527 | 454 | 371 | 212 | 120 | 37 | 4 | 2 | 1 | 247 | 224 | 194 | 157 | 91 | 50 | 17 | 2 | 2 | 1 | 325 | 293 | 250 | 205 | 115 | 65 | 19 | 2 |
| No pCR | 1403 | 1157 | 918 | 713 | 436 | 269 | 106 | 33 | 3 | 1 | 839 | 723 | 617 | 484 | 306 | 198 | 79 | 24 | 3 | 1 | 510 | 392 | 269 | 200 | 111 | 59 | 22 | 6 |



Number at risk

| | | | | | | | | | |
|--------|-----|-----|-----|-----|-----|-----|----|----|---|
| pCR | 389 | 349 | 310 | 250 | 166 | 88 | 29 | 11 | 1 |
| No pCR | 768 | 604 | 429 | 317 | 198 | 125 | 50 | 13 | 1 |

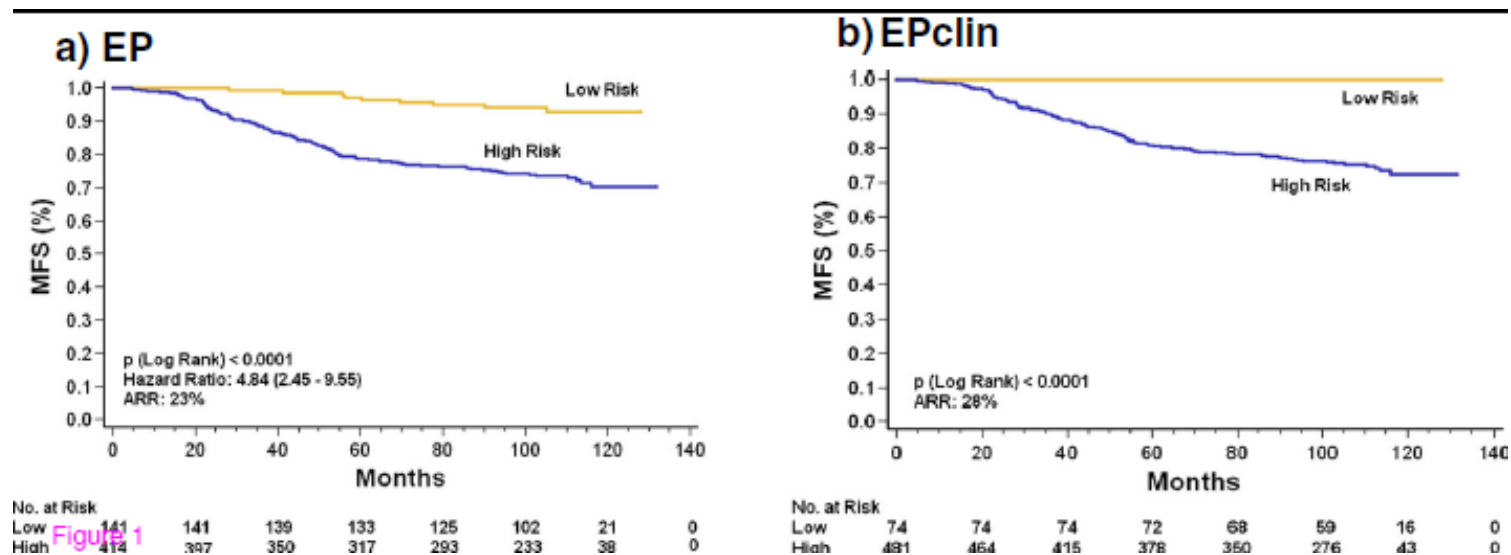
pCR/no pCR

Cortazar et al Lancet 2014

.org

Figure 5: Association between pCR and event-free survival, by breast cancer subtype

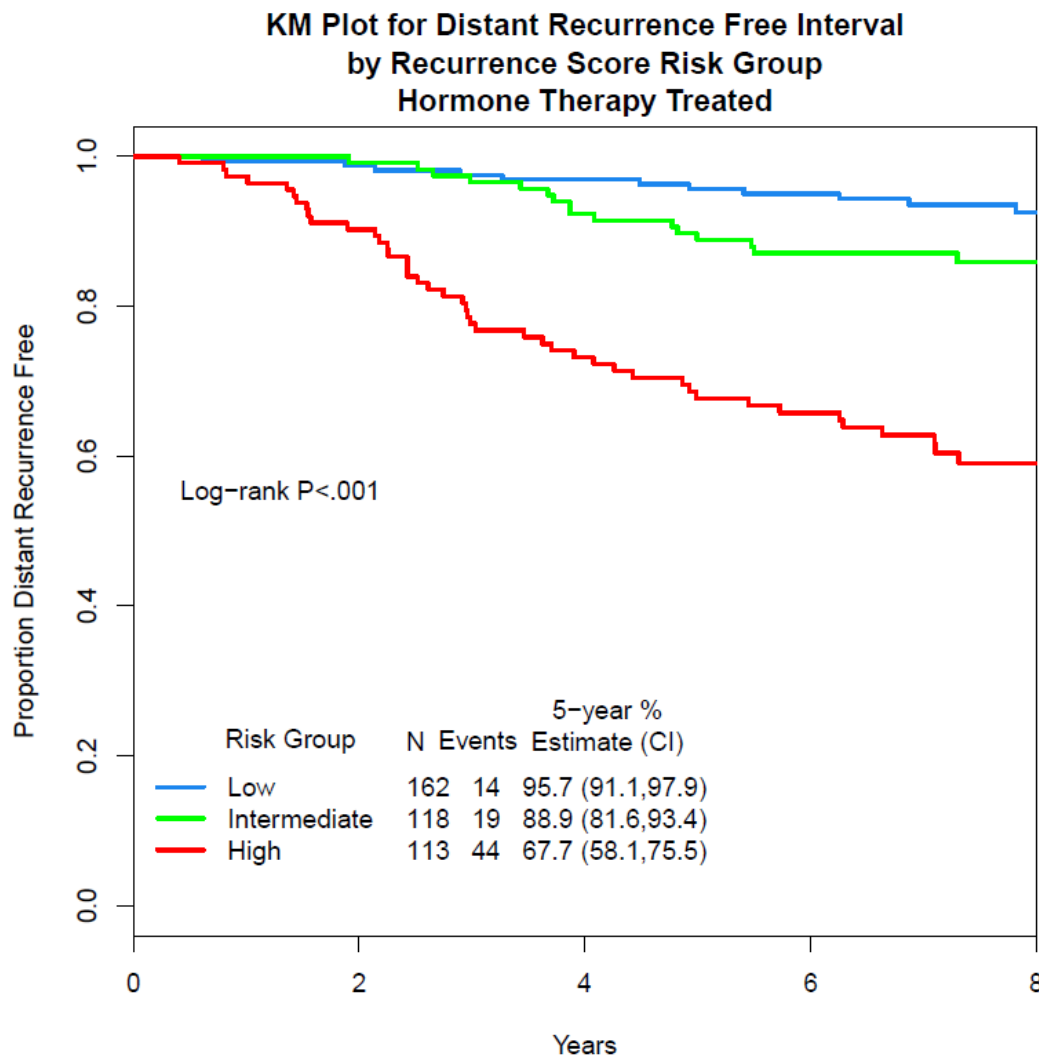
Search for predictors of relapse despite optimal treatment: adjuvant



GEICAM 9906- relapse risk despite optimal treatment
By Endopredict ® score

Martin et al BJC 2014

Search for predictors of relapse despite optimal treatment: adjuvant



PACS01- relapse risk
despite optimal
treatment
Accd to
OncotypeDX™

Penault Lorca et al, ASCO 2014

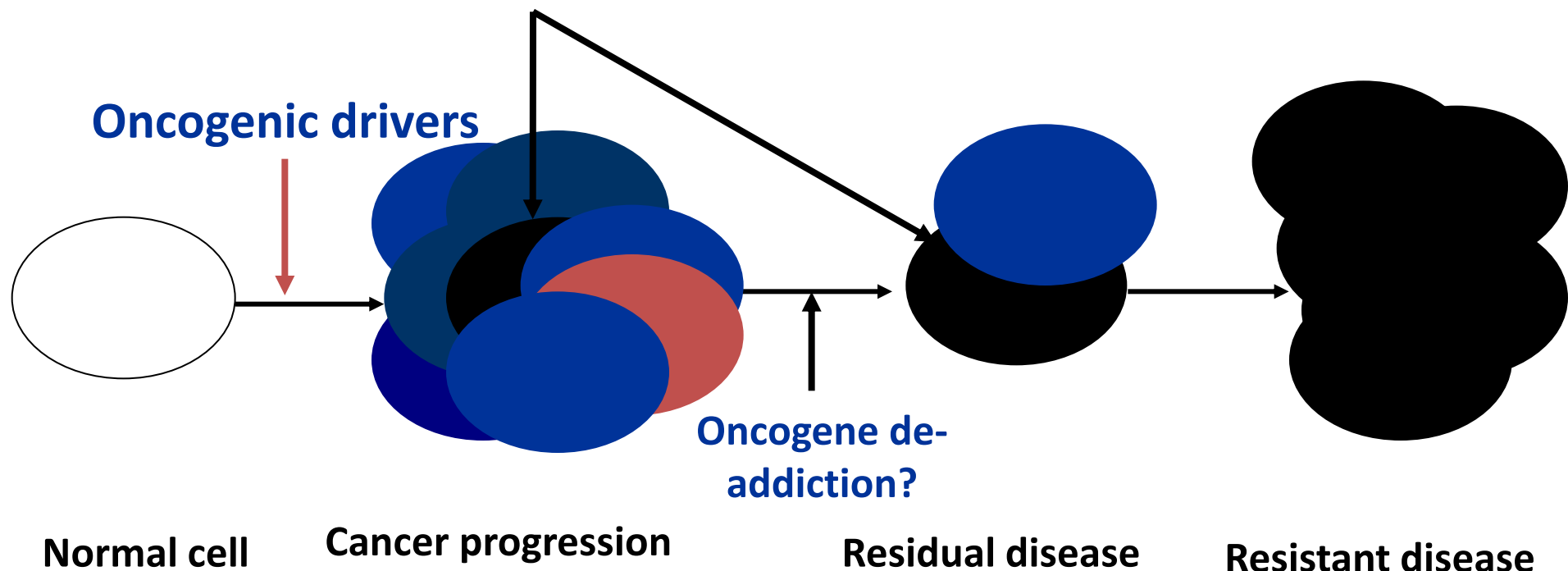
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- **Residual disease** appears as a potential/likely surrogate of metastatic spread (lethal clone?...) **PREDICTIVE VALUE?**

Residual tissue: does it contain lethal clones? Could it be a surrogate of metastatic spread???

Lethal subclone at diagnosis:
A minority clone present
at early stage, resistant to therapy
and leading to cancer death

From André et al, ASCO 2014



Normal cell

Cancer progression

Residual disease

Resistant disease

26-30 September 2014, Madrid, Spain

esmo.org

(Major) questions to be addressed today

1. How to better assess for residual disease and its prognostic value? F Symmans
2. How can we best characterize residual disease towards prognosis and prediction? F Penault Lorca
3. How can we best assess residual disease before surgery? A Makris
4. How to best address clinically the prognostic and predictive information derived from residual disease? A Tutt