Ovarian Cancer: Response followed by relapse – When will we shift the paradigm?

Moderator: Laura K. Shawver, PhD, Founder, The Clearity Foundation

Panelists:

Robert C. Bast, Jr., MD, Vice President for Translational Research, The University of Texas MD Anderson Cancer Center

Douglas A. Levine, MD, Head, Gynecology Research Laboratory, Associate Attending Surgeon, Gynecology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center

Geert Kolvenbag MD PhD, Global Product VP, Olaparib, AstraZeneca

Ovarian cancer by the numbers

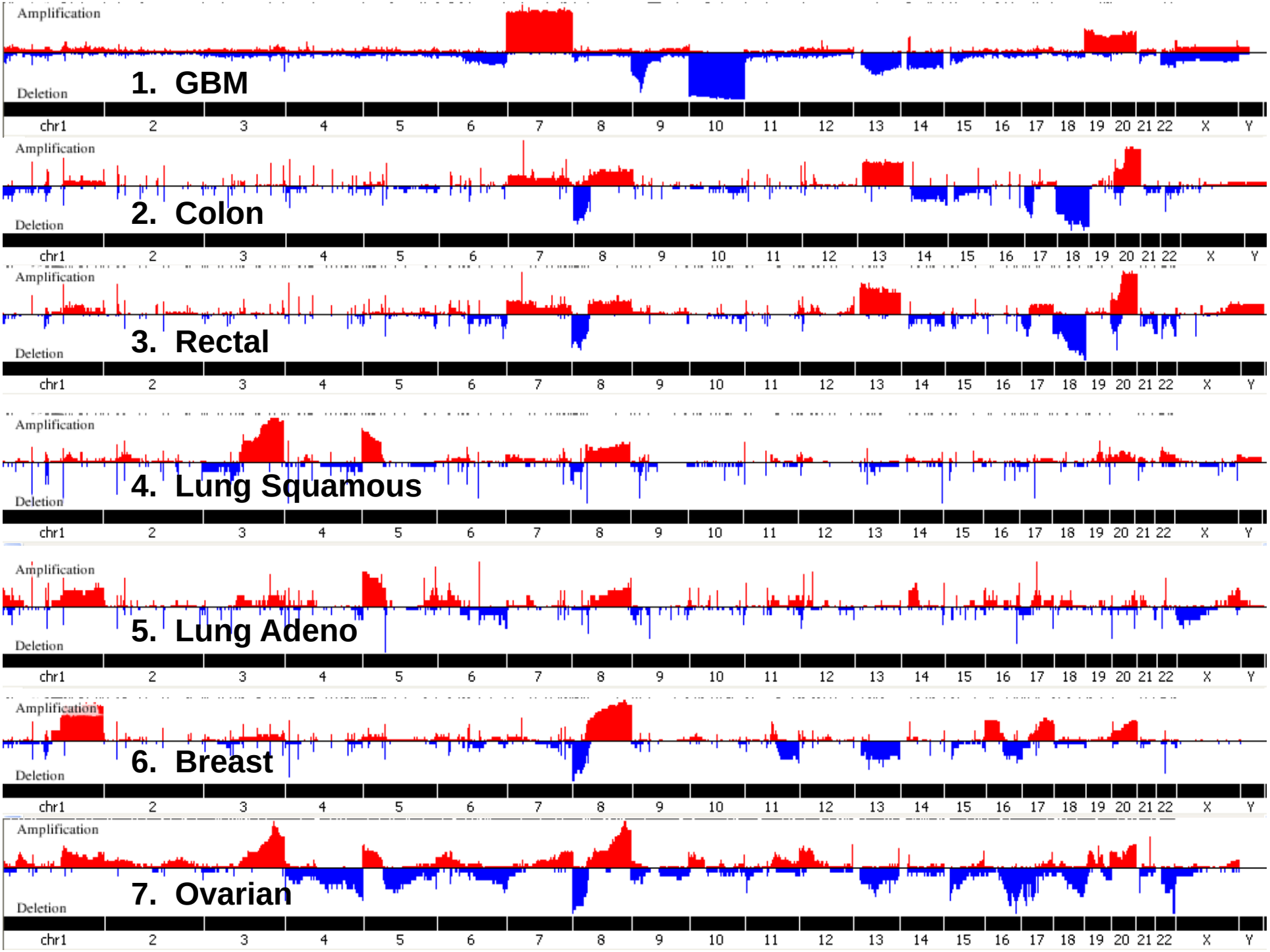
- 1.8% of women will develop ovarian cancer
- 21,600 new cases diagnosed in the US every year
- 15,000 women die each year from ovarian cancer

- 75% of ovarian cancer patients are diagnosed in Stage III or IV
- 75+% response to standard platinum/taxane treatment
- 75% recurrence rates (50% are within two years)

NCCN Guidelines for Epithelial Ovarian Cancer/Fallopian Tube Cancer/Peritoneal Cancer 2.2.2011

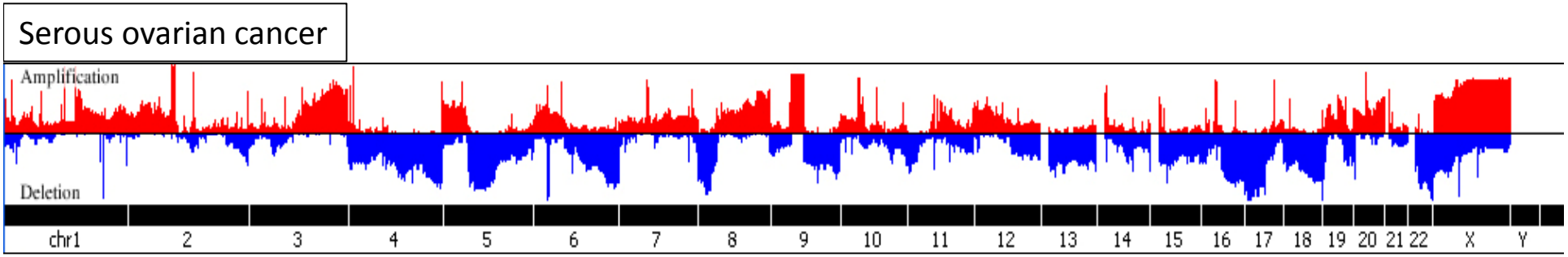
ACCEPTABLE RECURRENCE THERAPIES (1 of 2)[1]

Agents	Cytotoxic Therapy	Hormonal Therapy	Targeted Therapy	Radiation Therapy
Preferred Agents	<u>Combination if platinum sensitive</u> Carboplatin/paclitaxel (category 1)[2,3] Carboplatin/weekly paclitaxel[2,4] Carboplatin/docetaxel[2,5,6] Carboplatin/gemcitabine[2,7] Carboplatin/liposomal doxorubicin[2,8] Cisplatin/gemcitabine[2,9] <u>Single-agent if platinum sensitive</u> Carboplatin[7] Cisplatin[7] <u>Single-agent non-platinum based if platinum resistant</u> Docetaxel[10] Etoposide, oral[11] Gemcitabine[12,13] Liposomal doxorubicin[12,13] Paclitaxel, weekly[14] Topotecan[15]		Bevacizumab	
Other Potentially Active Agents	<u>Single Agents</u>[16] Altretamine Capecitabine Cyclophosphamide Ifosfamide Irinotecan Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound (nab-paclitaxel) Pemetrexed Vinorelbine	Anastrozole Letrozole Leuprolide acetate Megestrol acetate Tamoxifen		Palliative localized radiation therapy


Amplification
Deletion
1. GBM
chr1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y
Amplification
Deletion
2. Colon
chr1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y
Amplification
Deletion
3. Rectal
chr1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y
Amplification
Deletion
4. Lung Squamous
chr1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y
Amplification
Deletion
5. Lung Adeno
chr1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y
Amplification
Deletion
6. Breast
chr1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y
Amplification
Deletion
7. Ovarian
chr1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y

Heterogeneity of ovarian cancer

Genomic alterations observed in nearly every chromosome



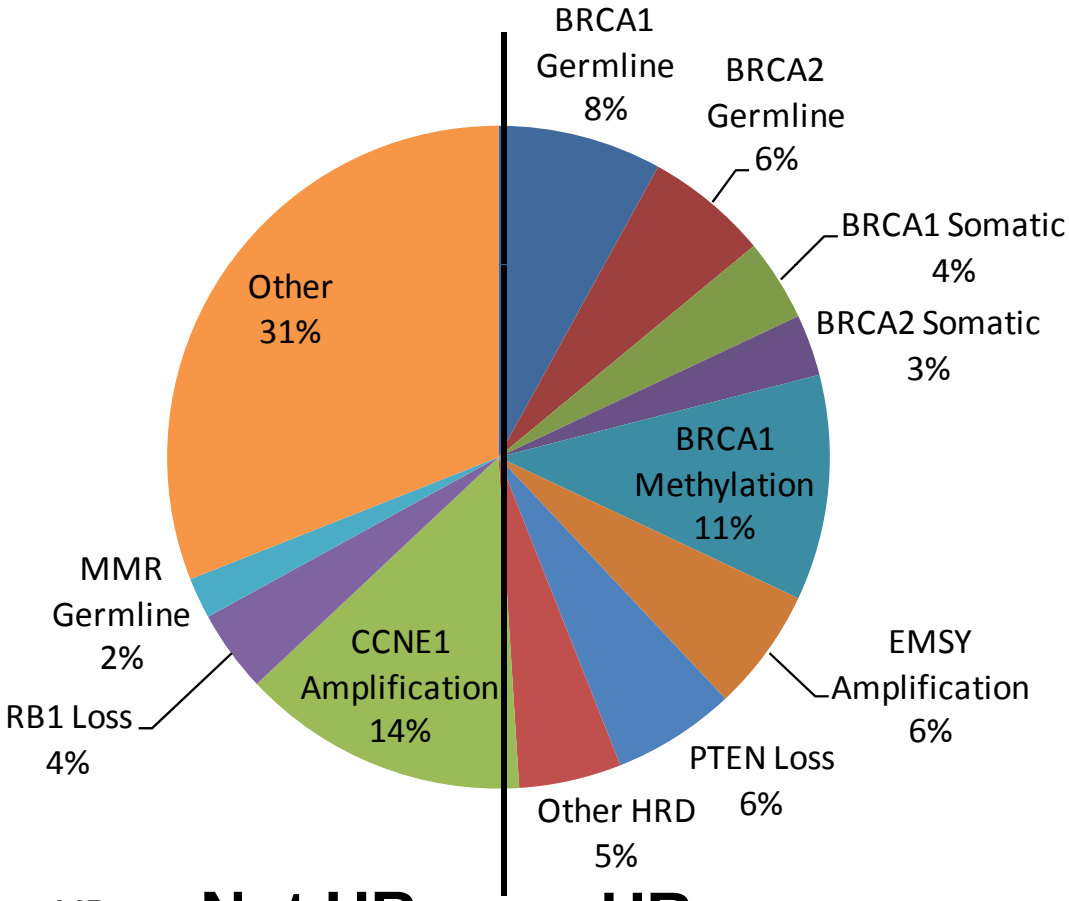
Key questions

- How do we segment the population for development and ultimately treatment?
- What will incentivize industry to pursue genetic subsets in ovarian cancer?
- How much emphasis should be placed on detection and prevention?

Data provided by Dr. D. Levine

Where does genomic instability come from?

Mutually exclusive events



Created by Douglas A. Levine, MD from data posted on the cBio Cancer Genomics Portal, MSKCC

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