

Expert Call – Innovation in Ovarian Cancer

Hosted by John Sonnier, William Blair

December 13, 2016

Forward-Looking Statements

This presentation includes forward-looking statements based on management's current expectations. These statements include, but are not limited to, ImmunoGen's expectations related to: the occurrence, timing and outcome of potential pre-clinical, clinical and regulatory events related to the Company's and its collaboration partners' product programs; the presentation of preclinical and clinical data on the Company's and its collaboration partners' product candidates; and the financial guidance provided. For these statements, ImmunoGen claims the protection of the safe harbor for forward-looking statements provided by the Private Securities Litigation Reform Act of 1995. Various factors could cause ImmunoGen's actual results to differ materially from those discussed or implied in the forward-looking statements, and you are cautioned not to place undue reliance on these forward-looking statements, which are current only as of the date of these slides. Factors that could cause future results to differ materially from such expectations include, but are not limited to: the timing and outcome of ImmunoGen's and its collaboration partners' research and clinical development processes; the difficulties inherent in the development of novel pharmaceuticals, including uncertainties as to the timing, expense and results of preclinical studies, clinical trials and regulatory processes; ImmunoGen's ability to financially support its product programs; the Company's dependence on its collaborative partners; industry merger and acquisition activity; and other factors more fully described in ImmunoGen's Annual Report on Form 10-K for the fiscal year ended June 30, 2016 and other reports filed with the Securities and Exchange Commission.

Update in the Treatment of Ovarian Cancer

Ursula Matulonis, M.D.
Director and Program Leader
Gynecologic Oncology Program
Dana-Farber Cancer Institute
Professor of Medicine
Harvard Medical School
Boston MA

Ovarian Cancer

(including fallopian tube and peritoneal cancer)

United States 2016 incidence and mortality:

- 22,280 new cases/yr
- 14,240 deaths/yr
- 1.3% lifetime risk of developing ovarian cancer

Death rates have been falling on average 2.2% each year over 2004-2013;

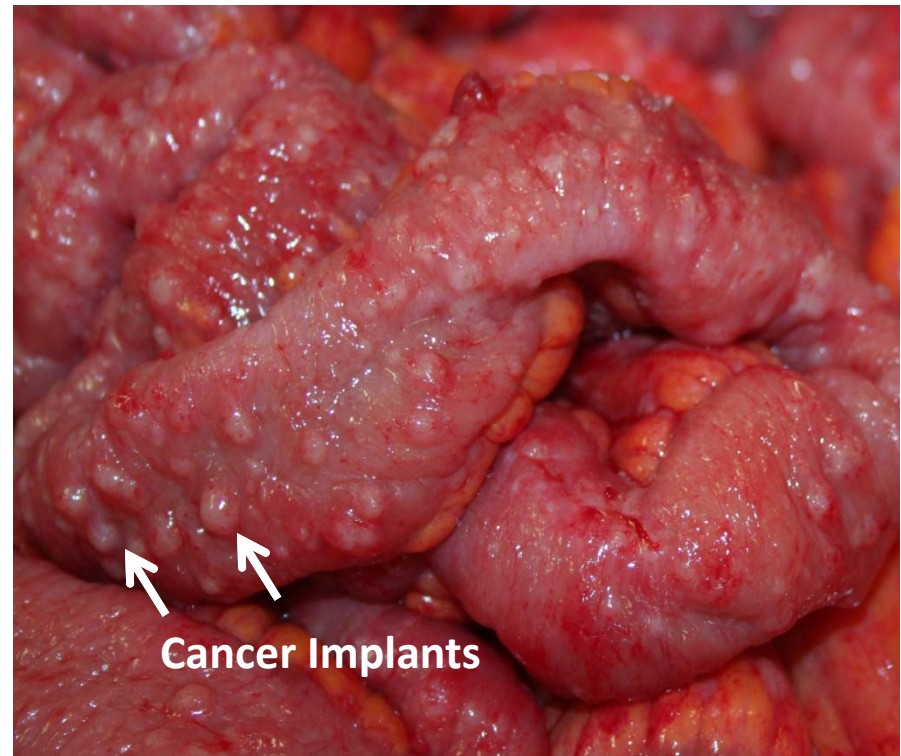
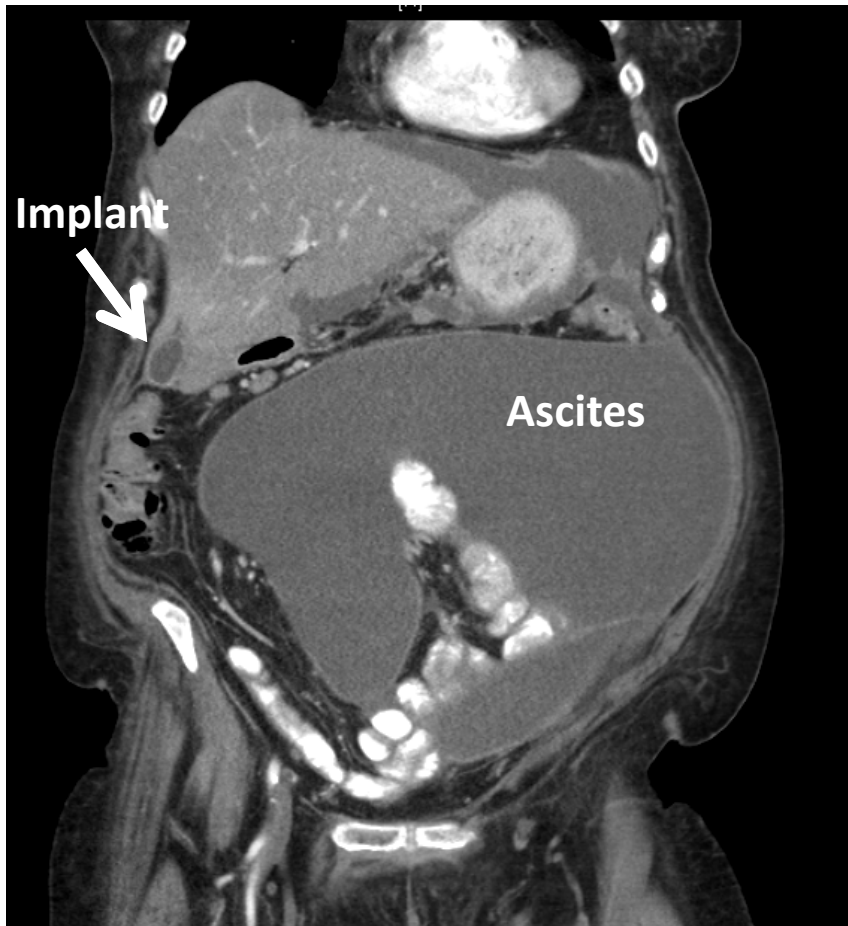
5 yr survival rates:

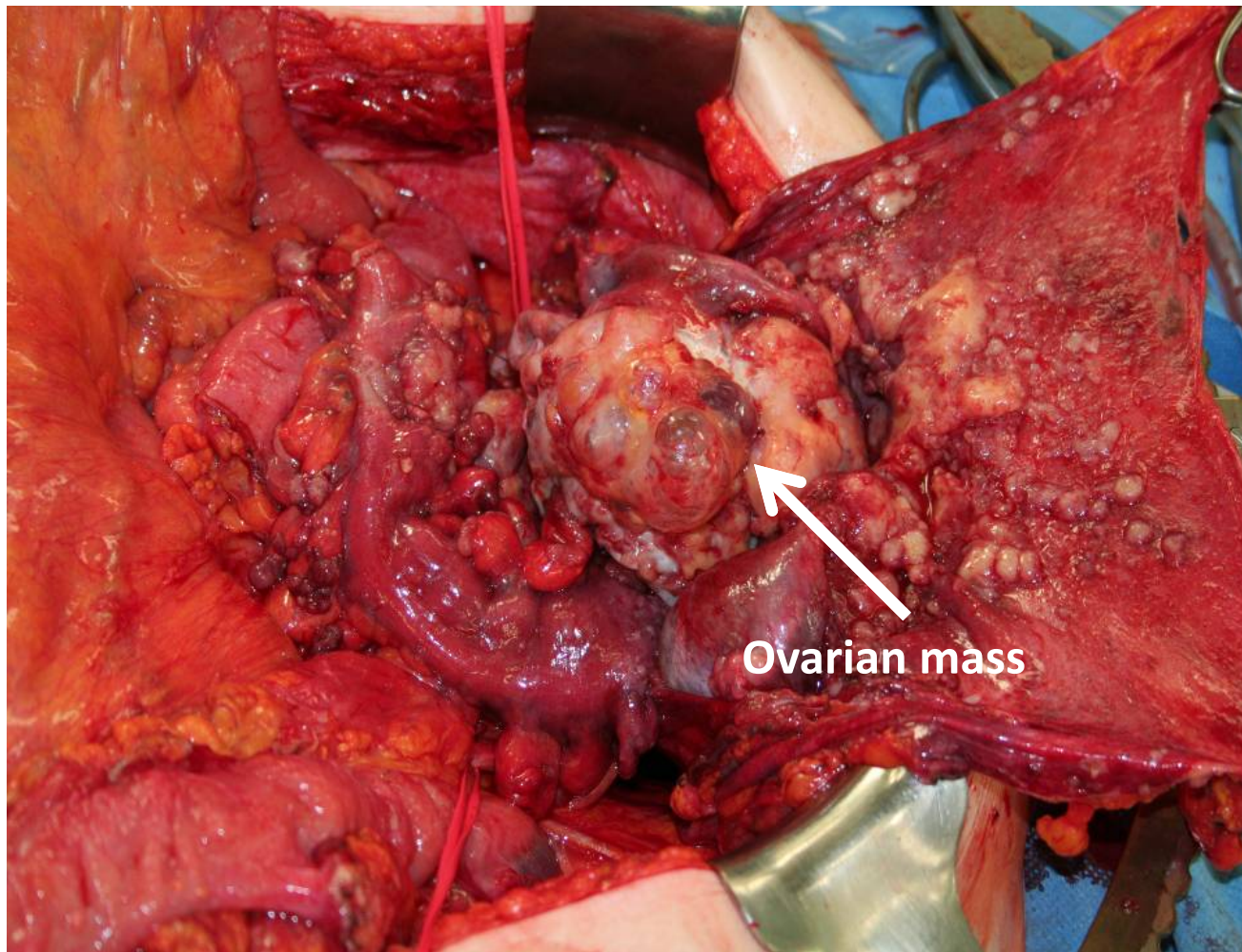
1975 33.7%

1990 40.4%

2008 46.2%

Most patients present with advanced cancer stage III or IV cancer characterized by peritoneal carcinomatosis and ascites





Basic principles of management

- Surgery should be performed by a gynecologic oncologist resulting in improved survival¹
- Decision made by gynecologic oncology surgeon for upfront surgery vs NACT (neoadjuvant chemotherapy)²
- Extent of debulking is what is left behind following completion of surgery.
- >1 cm of residual tumor is termed “suboptimal” cytoreduction
- ≤1 cm is termed “optimal” cytoreduction
- R0 is no evidence of gross residual cancer
- Distinctions are important for prognosis and treatment planning

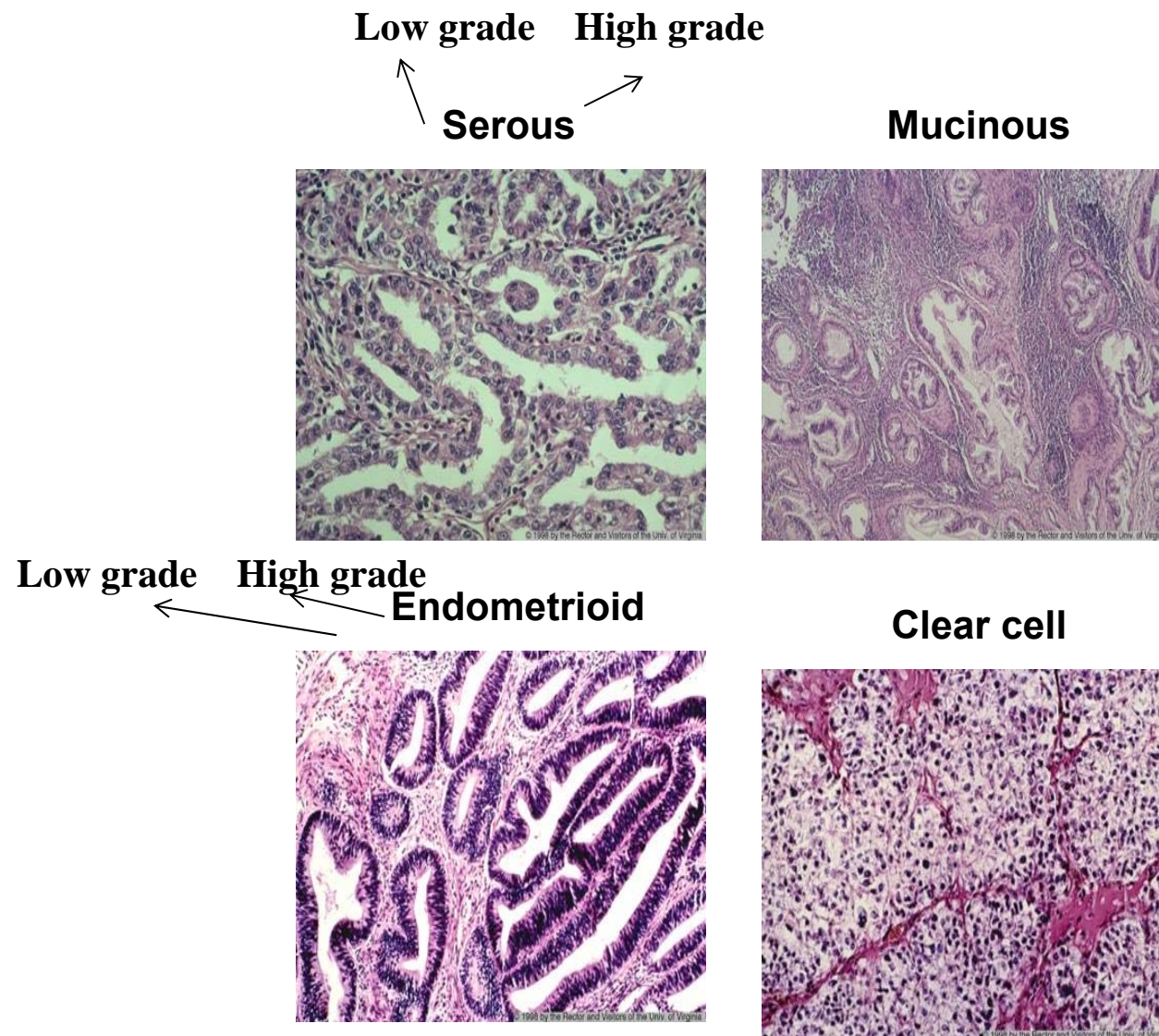
¹Elit et al, Gynecologic Oncology 87(3):260-7, 2002

²Wright et al, SGO and ASCO Neoadjuvant chemotherapy guidelines (asco.org and sgo.org)

Chemotherapy for Newly Diagnosed Ovarian Cancer

- Improvements in Overall Survival have been achieved with:
 - 1) Addition of every-3-wk paclitaxel to platinum
 - 2) Use of weekly paclitaxel (dose dense) compared with every-3-wk paclitaxel
- Use of IP chemotherapy in optimally cytoreduced pts (< 1 cm residual) has recently been placed into question by GOG 252 results
- Neoadjuvant chemotherapy (NACT): 2 randomized trials showed similar outcome (PFS, OS) as with upfront surgery, with *fewer* post-op deaths and grade 3/4 toxicities. Patients able to undergo primary debulking surgery should be offered NACT
- Addition of bevacizumab to carboplatin and paclitaxel → bev maintenance results in improvement in PFS but not OS in 2 randomized trials
- Additional maintenance strategies
 - Paclitaxel improves PFS, trend in OS but with unacceptable toxicity
 - Pazopanib – improves PFS, but not OS, also unacceptable toxicity
 - Olaparib – PAOLA (bev/olap vs bev) and SOLO-1 (olap vs placebo) are ongoing
 - Avelumab – JAVELIN paclitaxel/carboplatin +/- avelumab → +/- maintenance avelumab is ongoing

Ovarian cancer is separated into histological categories



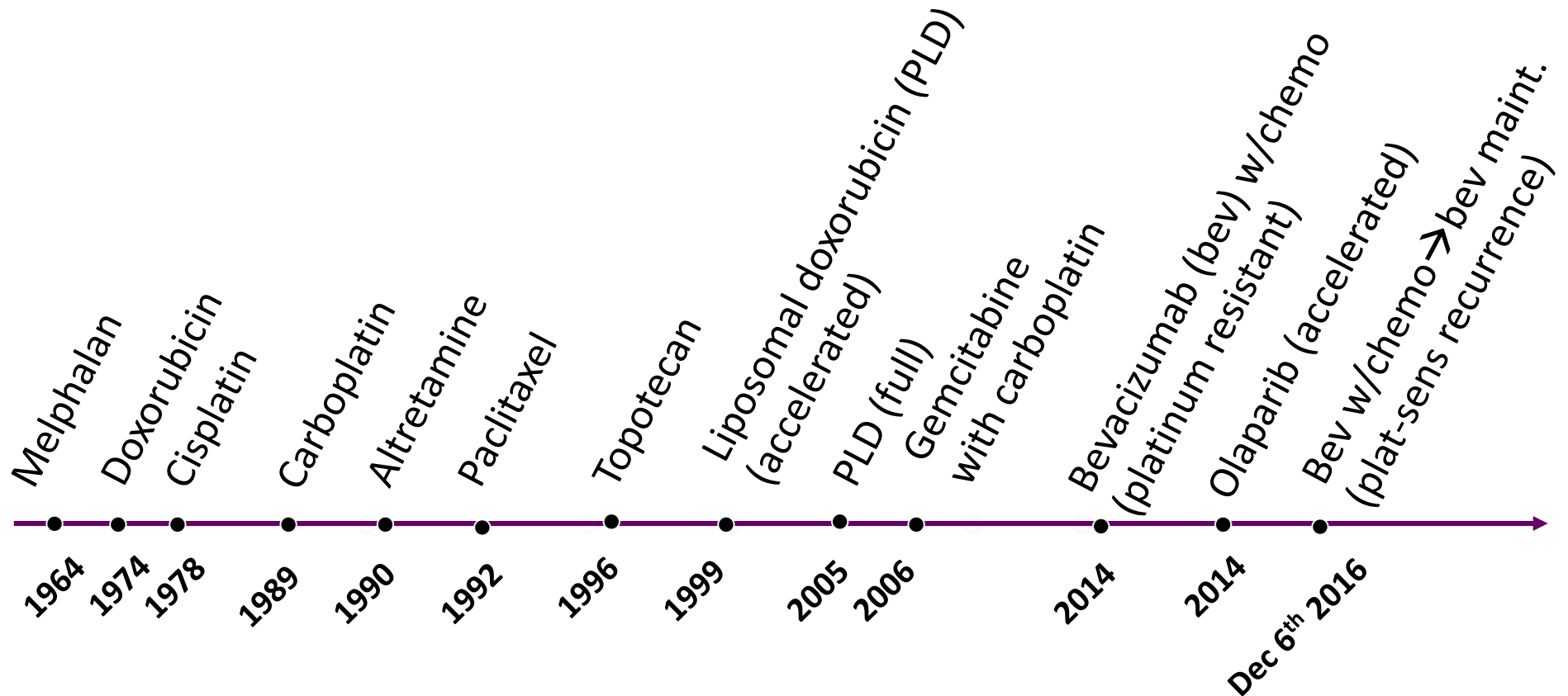
NCCN Genetic/Familial High-Risk Assessment

- NCCN Genetic/Familial High-Risk Assessment guidelines recommend the following individuals be referred to a cancer genetics professional for further genetic risk evaluation (including peritoneal and tubal cancers)
 - Known mutation in a gene associated with breast cancer susceptibility
 - Early onset breast cancer
 - Triple-negative breast cancer
 - ≥ 1 family member on the same side with a combination of breast cancer and 1 or more additional cancer
 - Ovarian cancer: **All patients should be offered testing!**
 - Male breast cancer

Recurrent Ovarian Cancer

- Most of patients with advanced epithelial ovarian cancer will eventually recur
- Detected mostly by asymptomatic rises in the CA125 level
- Recurrence is divided into:
 - Platinum refractory: growth on platinum or within one month
 - Platinum resistant: growth within 6 months of platinum
 - Platinum sensitive: cancer growth >6 months after platinum

Approved Drugs in Ovarian Cancer



Recommended Therapies for Recurrence of Ovarian Cancer

- **Platinum-sensitive disease**
 - Carboplatin
 - Carboplatin/docetaxel
 - **Carboplatin/gemcitabine**
 - Carboplatin/gemcitabine/
bevacizumab (category 2B)
 - **Carboplatin/liposomal
doxorubicin (category 1)**
 - **Carboplatin/paclitaxel
(category 1)**
 - Carboplatin/paclitaxel (weekly)
 - Cisplatin
 - Cisplatin/gemcitabine
 - Targeted therapy
 - Bevacizumab
 - **Olaparib**

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- Carboplatin/gemcitabine/bevacizumab (category 2B)
- **Carboplatin/liposomal doxorubicin (category 1)**
- **Carboplatin/paclitaxel (category 1)**
- Carboplatin/paclitaxel (weekly)
- Cisplatin
- Cisplatin/gemcitabine
- Targeted therapy
 - Bevacizumab
 - **Olaparib**

- **Platinum-resistant disease**

- Docetaxel
- Etoposide, oral
- Gemcitabine
- **Liposomal doxorubicin**
- **Liposomal doxorubicin/bevacizumab**
- **Paclitaxel (weekly)**
- **Paclitaxel (weekly)/bevacizumab**
- **Topotecan**
- **Topotecan/bevacizumab**
- Targeted therapy
 - Bevacizumab
 - **Olaparib**

Recurrent Ovarian Cancer

- Recurrent platinum sensitive disease - maintenance
 - Niraparib
 - Bevacizumab
- Olaparib – for patients with germline BRCA+ ovarian cancer who have received ≥ 3 prior lines of therapy
- Platinum resistant disease
 - Single agent cytotoxic chemotherapy
 - Combination with bevacizumab
 - Novel agents on the horizon

Recurrent Platinum-Sensitive Ovarian Cancer Maintenance Setting

- Niraparib
 - NOVA – Switch-maintenance therapy with niraparib superior to placebo¹
 - Greatest benefit in gBRCA+ subset, ~20% population, but benefit observed in all subgroups of patients
 - Rolling NDA submitted 12 Sep 2016
- Bevacizumab
 - As part of a combination regimen with chemotherapy followed by bev maintenance
 - OCEANS² – PFS without OS benefit
 - GOG-0213³: Five month improvement in OS
 - FDA Approved Dec 6th 2016

¹Mirza et al., NEJM 2016

²Aghajanian et al., JCO 2012

³Coleman et al., SGO 2015 Abs 3; GNE
press release 06Dec16

Olaparib Monotherapy in germline *BRCA*+ Advanced Ovarian Cancer

- Pts had received ≥ 3 prior lines of therapy,
- Regardless of platinum sensitivity

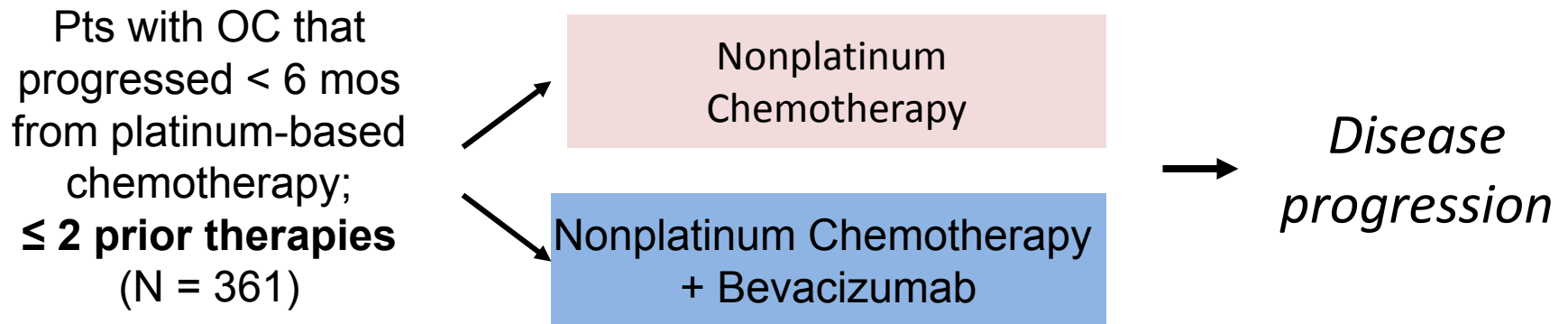
<u>Response</u>	<u>N = 137</u>
Objective response rate, % (95% CI)	34 (26-42)
CR, %	2
PR, %	32
Median DOR, mos (95% CI)	7.9 (5.6-9.6)

Olaparib [package insert].

Toxicities are gastrointestinal (nausea, vomiting, abdominal pain, anorexia) and hematologic (anemia, thrombocytopenia)

Recommended dose is 400 mg PO BID (capsule formulation)

AURELIA: Phase III Nonplatinum Chemotherapy ± Bevacizumab in recurrent platinum resistant ovarian cancer



mPFS 3.4 → 6.7 months
HR 0.48, p<0.001

Chemotherapy options:

- Paclitaxel 80 mg/m² on Days 1,8,15, 22 every 28 days
- Topotecan 4 mg/m² on Days 1, 8 ,15 every 28 days or
- Topotecan 1.25 mg/m² on Days 1-5 every 21 days
- Pegylated liposomal doxorubicin (PLD) 40 mg/m² on Day 1 every 28 days

AURELIA: most pronounced effect on PFS and OS when bev added to weekly paclitaxel

	<u>PLD</u>	<u>PLD/ bev</u>	<u>Weekly paclitaxel</u>	<u>Weekly Pac/bev</u>	<u>Topotecan</u>	<u>Topo/bev</u>
RR	7.8%	13.7%	30.2%	53.3%	0%	17%
PFS (median)	3.5 mos	5.4 mos	3.9 mos	10.4 mos	2.1 mos	5.8 mos
OS (median)	14.1 mos	13.7 mos	13.2 mos	22.4 mos	13.3 mos	13.8 mos

Close to 40% of patients in each group of chemotherapy alone crossed over to bev following progression.

PLD = pegylated liposomal doxorubicin

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Bevacizumab: FDA Approval in 2014

- Combined with either weekly paclitaxel, PLD or topotecan for platinum-resistant recurrent ovarian cancer
- Bevacizumab-containing doublets had higher total # of events of:
 - ≥ Grade 2 HTN
 - ≥ Grade 2 GIP
 - All grades proteinuria
 - ≥2 Grade fistula/abscess

Novel agents on the horizon for platinum resistant disease

- Rucaparib: NDA submitted Aug 2016 for germline and somatic *BRCA*
- Checkpoint inhibitors
- Olaparib/cediranib
- Lurbinectedin
- Fosbretabulin
- Mirvetuximab soravtansine

Conclusions

- Significant unmet needs remain in patients with recurrent ovarian cancer

There is a need to:

- lengthen time to recurrence and improve overall survival, without negatively impacting quality of life or causing toxicities limiting subsequent therapies
- Develop targeted therapies for subsets of ovarian cancer patients other than those with BRCA mutations or those with HRD characteristics



Mirvetuximab Soravtansine

Positioned for Pivotal Development in Ovarian Cancer

Kathleen Moore, M.D.

*Associate Professor of Section of Gynecologic Oncology and
Director of Oklahoma TSET Phase I Program at the Stephenson Cancer Center*



Overview

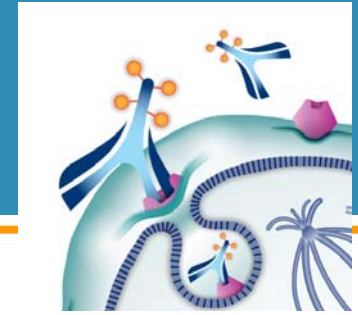
- Unmet needs in ovarian cancer
- Introduction to mirvetuximab soravtansine
- Ovarian cancer treatment landscape, highlighting opportunities for mirvetuximab soravtansine
- Recap of phase 1 data for mirvetuximab soravtansine
- Next steps
 - Pivotal phase 3 study in platinum resistant ovarian cancer
 - Combinations to move into earlier lines of therapy

The Unmet Needs in Ovarian Cancer

- In platinum-resistant disease ($\geq 2^{\text{nd}}$ line):
 - Current single-agent therapies:
15-20% ORR¹; 3.5 – 4 months mPFS¹
 - US²: 19,500 EU²: 24,000
 - More effective and well tolerated monotherapy
 - More effective combination therapy
- In platinum-sensitive disease ($\geq 2^{\text{nd}}$ line) :
 - US²: 7,500 EU²: 9,200
 - Lengthen time to recurrence without worsening QOL or increasing toxicities that might limit subsequent therapies
 - Improved survival
 - Improved patient selection for maintenance therapy, especially for patients without BRCA mutations or HRD

¹ Published data and prescribing information; ²Decision Resources Group Patientbase
ORR: objective response rate; PFS: progression-free survival

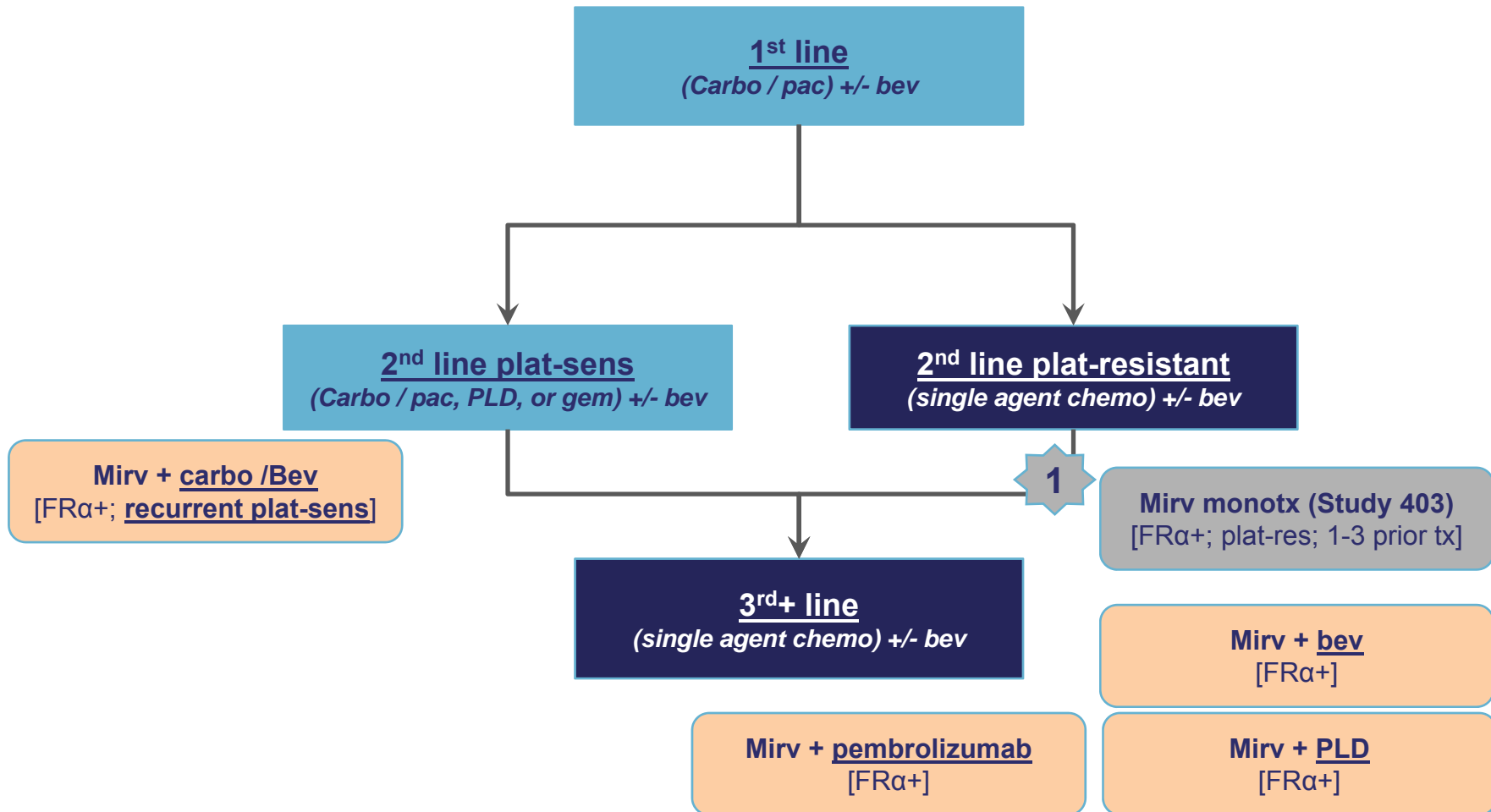
Mirvetuximab Soravtansine




- First ADC to enter registration testing for ovarian cancer
- MOA and target distinct from other approaches (PARPi, I/O)
- First indication – monotherapy in platinum-resistant disease
 - Fast to market strategy
- Subsequent indications – in combination, in earlier lines of therapy

Advanced Ovarian Cancer Patient Flow

Mirvetuximab soravtansine potential patient populations





Mirvetuximab Soravtansine

46 patient ovarian expansion cohort

K Moore, ASCO 2016, #5567

Accepted for publication in JCO, “in press”

Baseline Demographics

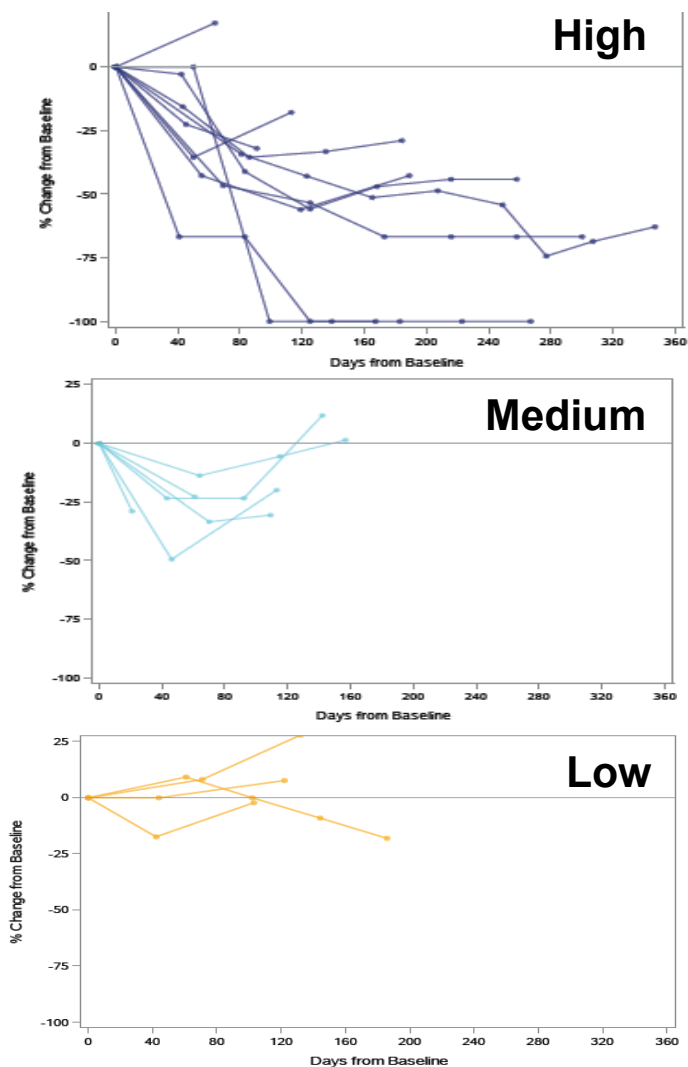
	Patients (n=46)	
Characteristic	No.	%
Age, years		
Median (range)	62.5	
Range	41-81	
Primary Diagnosis		
Epithelial ovarian cancer	40	87
Fallopian tube cancer	2	4
Primary peritoneal cancer	1	2
High grade Mullerian carcinoma	1	2
Serous and transitional cell carcinoma	1	2
Carinosarcoma	1	2
ECOG PS		
0	22	48
1	24	52
Number of prior systemic therapies		
1-3	23	50
4+	23	50
Prior Exposure		
Platinum compounds	46	100
Taxane	46	100
Bevacizumab	29	63

Mirvetuximab Soravtansine Shows Encouraging Activity in Patients with Platinum-Resistant Ovarian Cancer

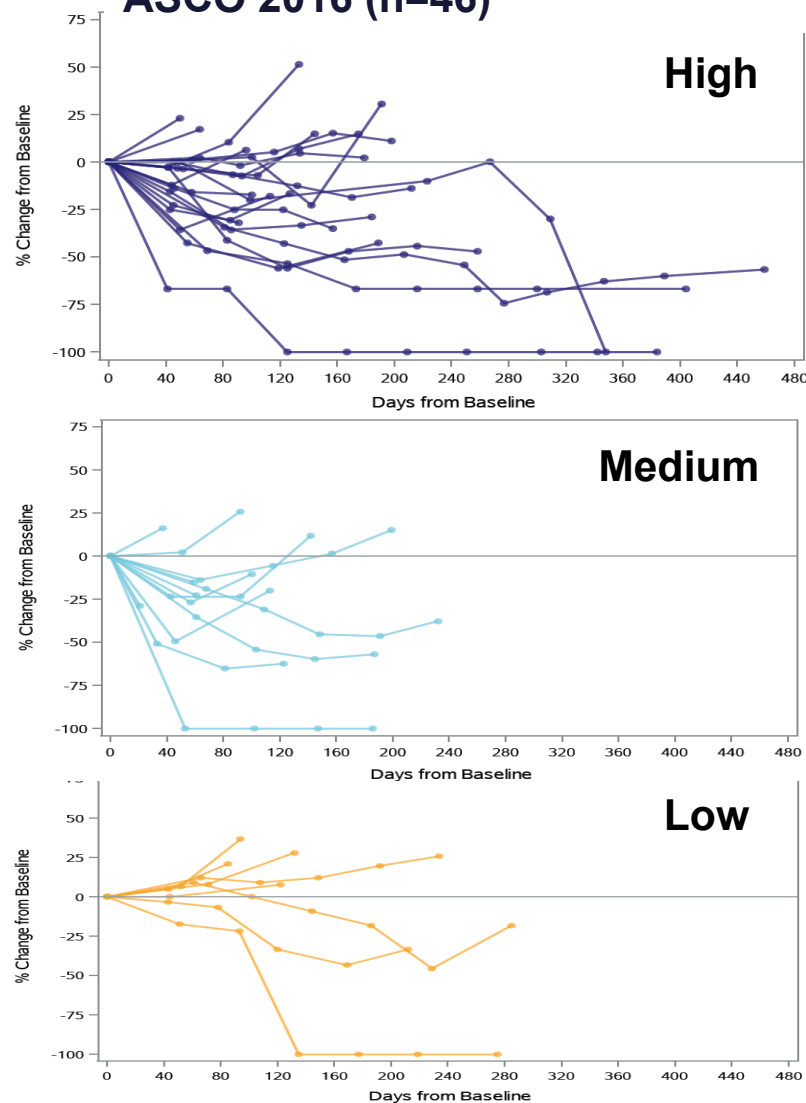
	All pts (n = 46)	1-3 priors + med/high FRa expression (n = 16)
Confirmed ORR 95% CI	26% (14, 41)	44% (20, 70)
PFS Median 95% CI	4.8 months (3.9, 5.7)	6.7 months (3.9, 11.0)
		Phase 3 study population

Deeper/Longer Tumor Shrinkage with Higher FR α Supports Using PFS as Primary Endpoint in Phase 3

AACR/NCI/EORTC 2015 (n=20)



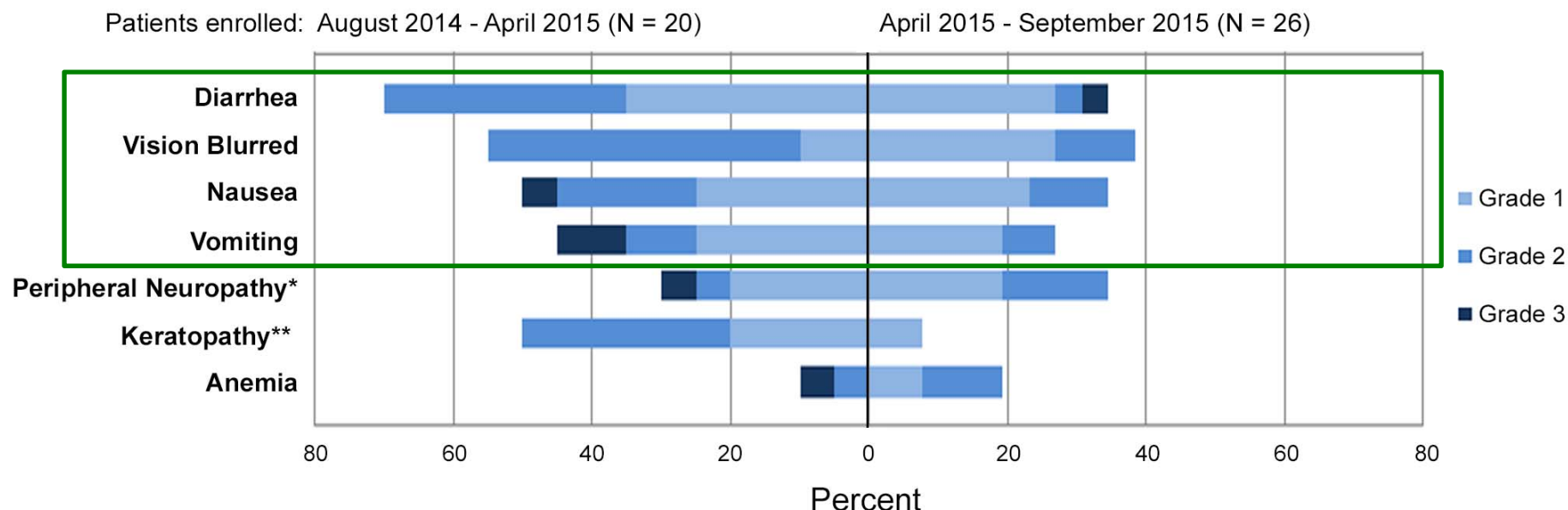
ASCO 2016 (n=46)



Based on measurable disease

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With Investigator Experience – Improved Safety Profile



*Includes Neuropathy peripheral, Peripheral sensory neuropathy, Peripheral motor neuropathy, Paraesthesia, and Hypoesthesia

**Includes Corneal cyst, Corneal disorder, Corneal deposits, Corneal epithelial microcysts, Keratitis, Keratopathy, Limbal stem cell deficiency, and Punctate keratitis

- ▶ Ocular and GI adverse events decreased in frequency and grade in the subset of 26 patients enrolled following the initial 20-patient cohort analyzed
 - This improvement may be due to investigator experience, the use of preservative-free lubricating eye drops and other measures mandated in April 2015 to manage such symptoms

Approved Monotherapies for Platinum Resistant Ovarian Cancer (PROC)

	ORR	mPFS/TTP (months)	Common AEs	References
Paclitaxel	6.7-30.2%	3.4-3.9	Hair loss, neuropathy	USPI; JCO (2015) 33(32):3836-3838
PLD (pegylated liposomal doxorubicin)	7.8-12.3%	2.1-3.7	Hand foot syndrome	USPI; JCO (2015) 33(32):3836-3838; Gyn Onc (2014) 133:624-631
Topotecan	0.0-19.3%	2.1-4.2	Low blood counts fatigue	USPI; JCO (2015) 33(32):3836-3838; Gyn Onc (2014) 133:624-631

Mirvetuximab Soravtansine – Promising Activity in PROC

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Mirvetuximab soravtansine				
• Overall pop	26%	4.8	Diarrhea	K Moore ASCO 2016 #5567
• Pts with 1-3 priors, med/high FR α	44%	6.7	Blurred vision	

GYN Steering Committee Members

Advisor	Institution	Country
Carol Aghajanian	MSKCC	USA
Michael Birrer	MGH	USA
Robert Coleman	MD Anderson	USA
Ursula Matulonis	DFCI	USA
Bradley Monk	University of Arizona	USA
Kathleen Moore	University of Oklahoma	USA
Andres Poveda	Fundacion Oncology Valencia	Spain
Ignace Vergote	Leuven Cancer Institute	Belgium

Single Agent Mirvetuximab Soravtansine Ready for Phase 3 Trial in Platinum Resistant Ovarian Cancer

- Compelling single agent activity – especially in patients with 1-3 priors and med/high FRα
- Well-tolerated – ocular and GI events generally low grade and easily managed
- Phase 3 trial designed to compare mirvetuximab soravtansine to approved monotherapies for platinum resistant ovarian cancer with rapid path to approval



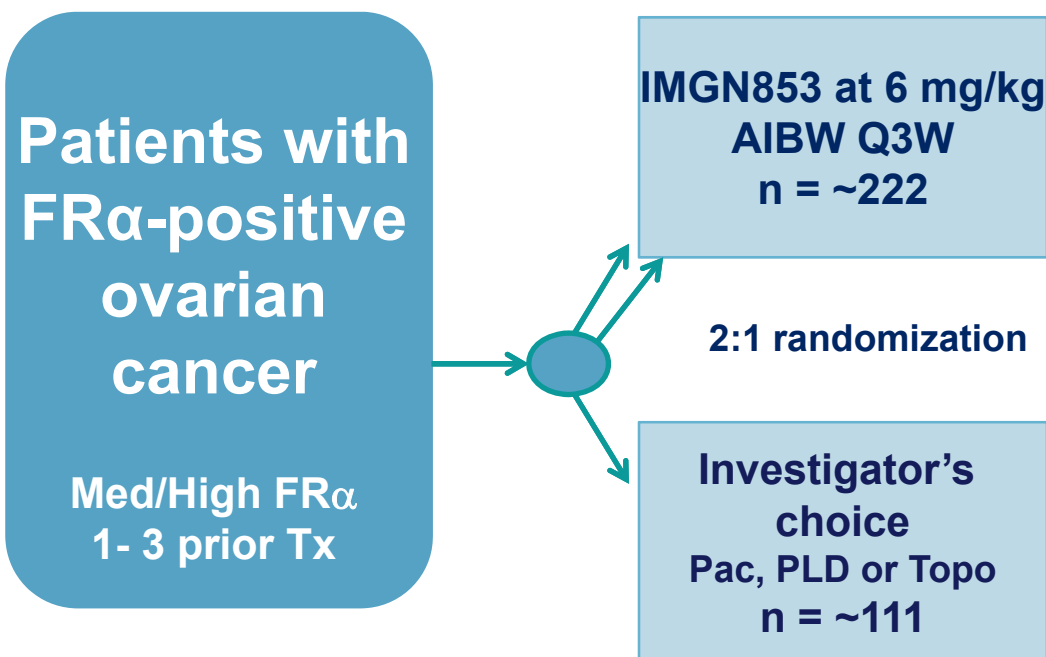
Mirvetuximab Soravtansine Phase 3 “FORWARD I” Trial in Ovarian Cancer

Mirvetuximab Soravtansine Registration Strategy

- Randomized phase 3 (vs investigator choice chemo) with PFS as primary endpoint in platinum-resistant FR α positive ovarian cancer with 1-3 prior lines of therapy
- One pivotal trial, designed to support full approval
- Robust safety database
 - Over 200 patients have received mirvetuximab sorvatansine as of 21 Nov 2016
- Straightforward design
 - FDA agreed with study endpoints and design



Phase 3 Trial Open for Enrollment



- **Primary endpoint : PFS** (blinded independent central review)
 - Entire population
 - Subset with high FR α (~2/3 of patients in study)
- **Secondary endpoints: ORR, DOR, QoL and OS**
- **Interim for futility at 80 events**

Pac: paclitaxel; PLD: pegylated liposomal doxorubicin; Topo: topotecan; AIBW = adjusted ideal body weight

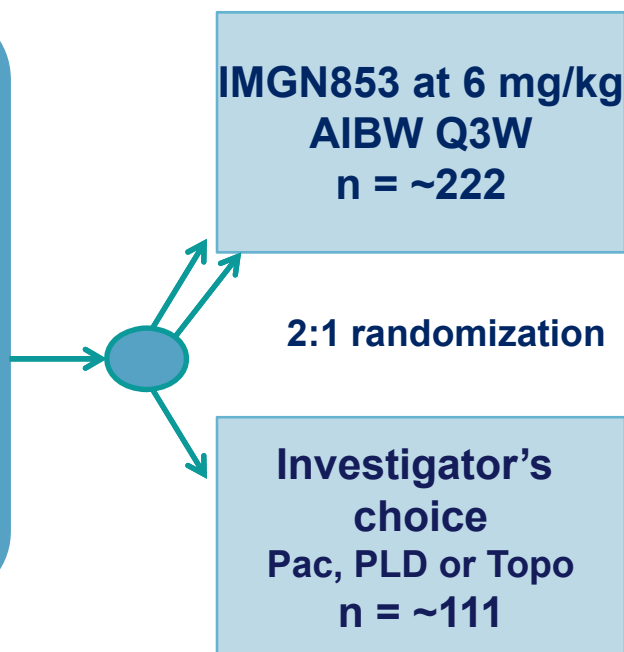
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Phase 3 Trial Open for Enrollment

**Patients with
FR α -positive
ovarian
cancer**

Med/High FR α
1- 3 prior Tx



- **Co-PIs:**
 - Kathleen Moore
 - Michael Birrer
- **Partnering with GOG Foundation**
- **> 100 sites in US, Canada, W. EU**

- **Primary endpoint : PFS** (blinded independent central review)
 - Entire population
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Mirvetuximab Soravtansine Combinations in Ovarian Cancer

**Patients with
FR α -positive
ovarian
cancer**

FR α \geq 25%
Plat resistant
Plat sens (carbo)

+ Bevacizumab

+ Carboplatin

+ PLD

+ Pembrolizumab

**Bev
expansion cohort**

**Pembro
expansion cohort**

- Data from dose escalation cohorts to be presented mid-2017
- Full labeled dose of combination agents reached
 - Bev and pembro expansion cohorts actively enrolling
- Enable mirvetuximab soravtansine to move up into earlier lines of therapy

*Preclinical combination data published – Ponte et al, Neoplasia 2016

Conclusions



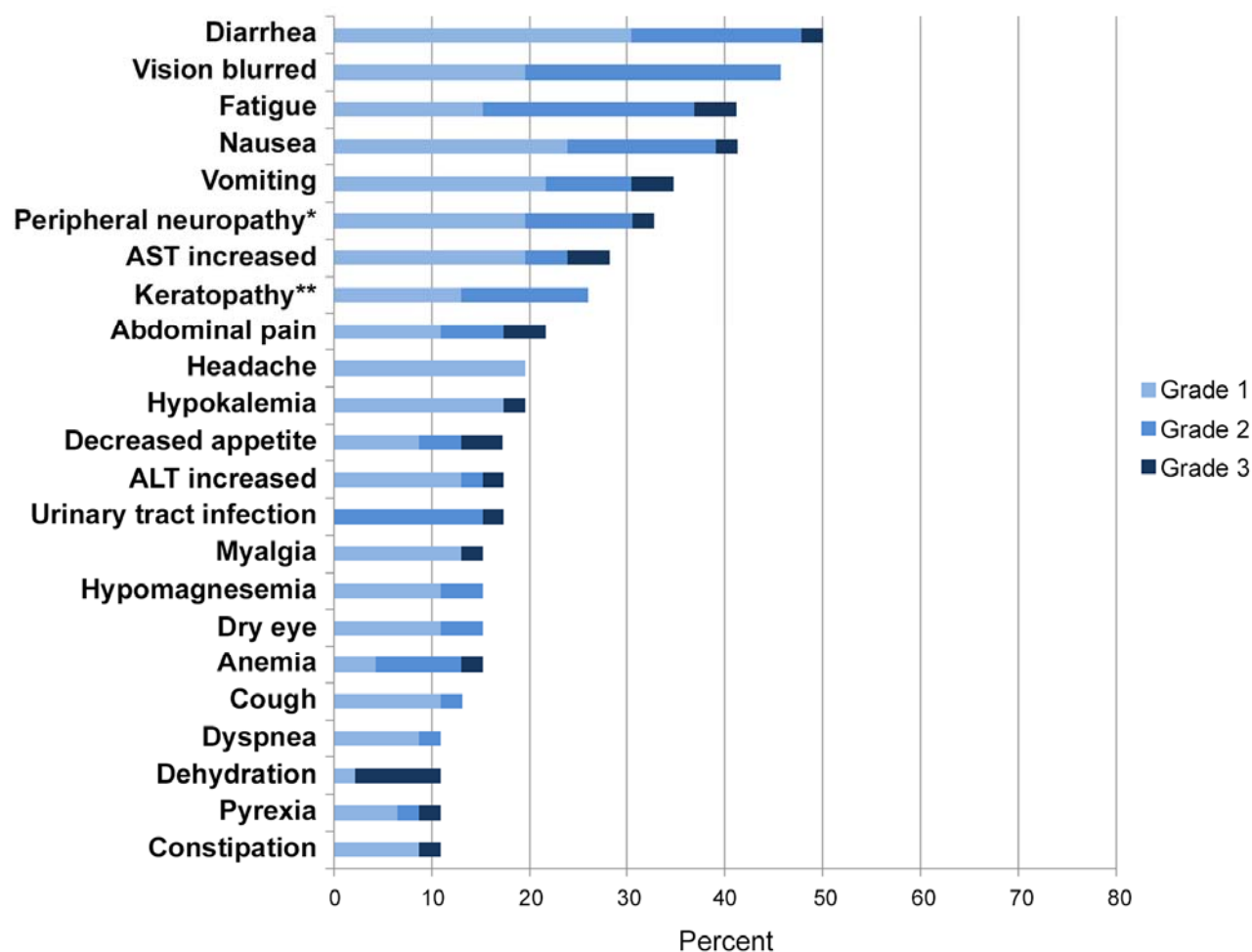
- Mirvetuximab soravtansine monotherapy is ready for phase 3
- Compelling single agent activity – especially in patients with 1-3 priors and med/high FR α
- Well-tolerated – ocular and GI events generally low grade and easily managed
- Consistency of data across cohorts supports phase 3 trial design
 - Larger sample size and longer follow-up in the initial and subsequent ovarian cancer cohorts confirm that mirvetuximab soravtansine is ready for phase 3
 - Expanded phase 1 data at SGO March 2017
 - Eye drop cohort to be presented later in 2017
- Phase 3 trial is open for enrollment
- Bevacizumab and pembrolizumab expansion cohorts are enrolling
- Combinations will enable mirvetuximab soravtansine to move up into earlier lines of therapy

Q&A



Back Up

Treatment Emergent Adverse Events > 10% (N = 46)



*Includes Neuropathy peripheral, Peripheral sensory neuropathy, Peripheral motor neuropathy, Paraesthesia, and Hypoesthesia

**Includes Corneal cyst, Corneal disorder, Corneal deposits, Corneal epithelial microcysts, Keratitis, Keratopathy, Limbal stem cell deficiency, and Punctate keratitis

Waterfall Plot and PFS

