MUCINOUS OVARIAN LESIONS CLINICAL PERSPECTIVE

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I DECLARE NO CONFLICT OF INTEREST

OBJECTIVES

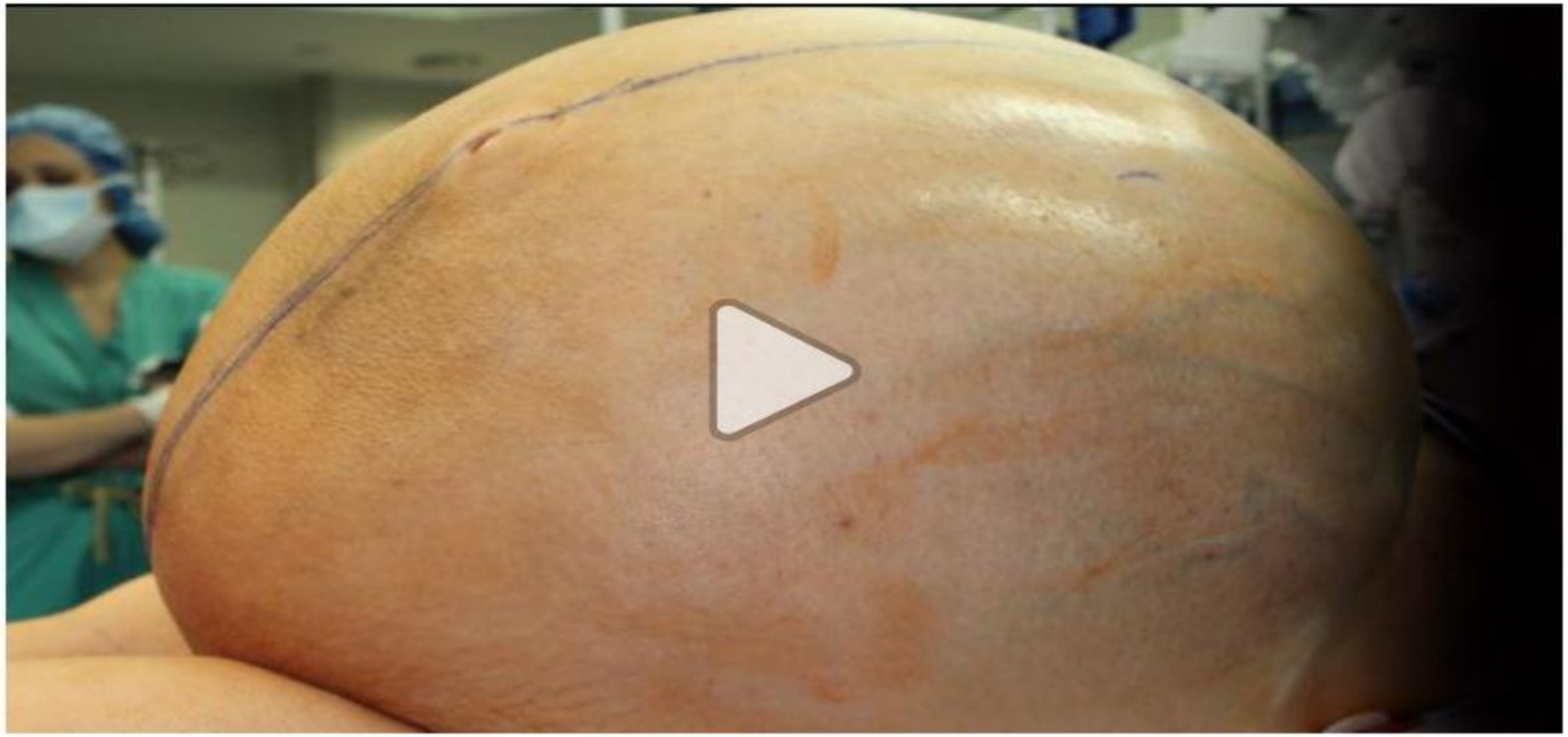
AT THE END OF THIS SESSION, PARTICIPANTS WILL BE ABLE TO

- UNDERSTAND THE UNIQUENESS OF MUCINOUS OVARIAN TUMOURS
- UNDERSTAND THE CHALLENGES IN THE DIAGNOSIS AND MANAGEMENT OF MUCINOUS OVARIAN TUMOURS
- BE UP TO DATE ON THE CURRENT RECOMMENDATIONS AND FUTURE DIRECTIONS IN THE CLINICAL MANAGEMENT OF MUCINOUS OVARIAN CANCER

132-pound ovarian tumor removed from Connecticut woman

By Mark Lieber, CNN

Updated 5:37 AM ET, Sat May 5, 2018



132-pound ovarian tumor removed from woman 01:07

Story highlights

(CNN) — A 132-pound ovarian tumor was removed from a 38-year-old Connecticut woman this year, according to

GYNECOLOGIC ONCOLOGY 54, 365–371 (1994)

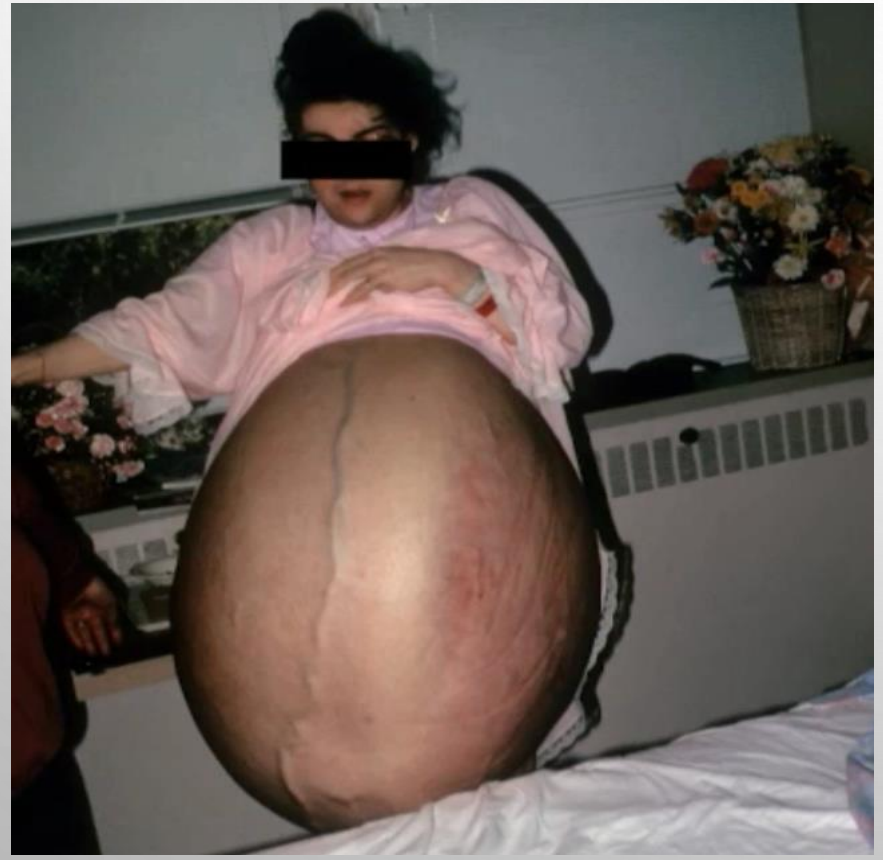
CASE REPORT

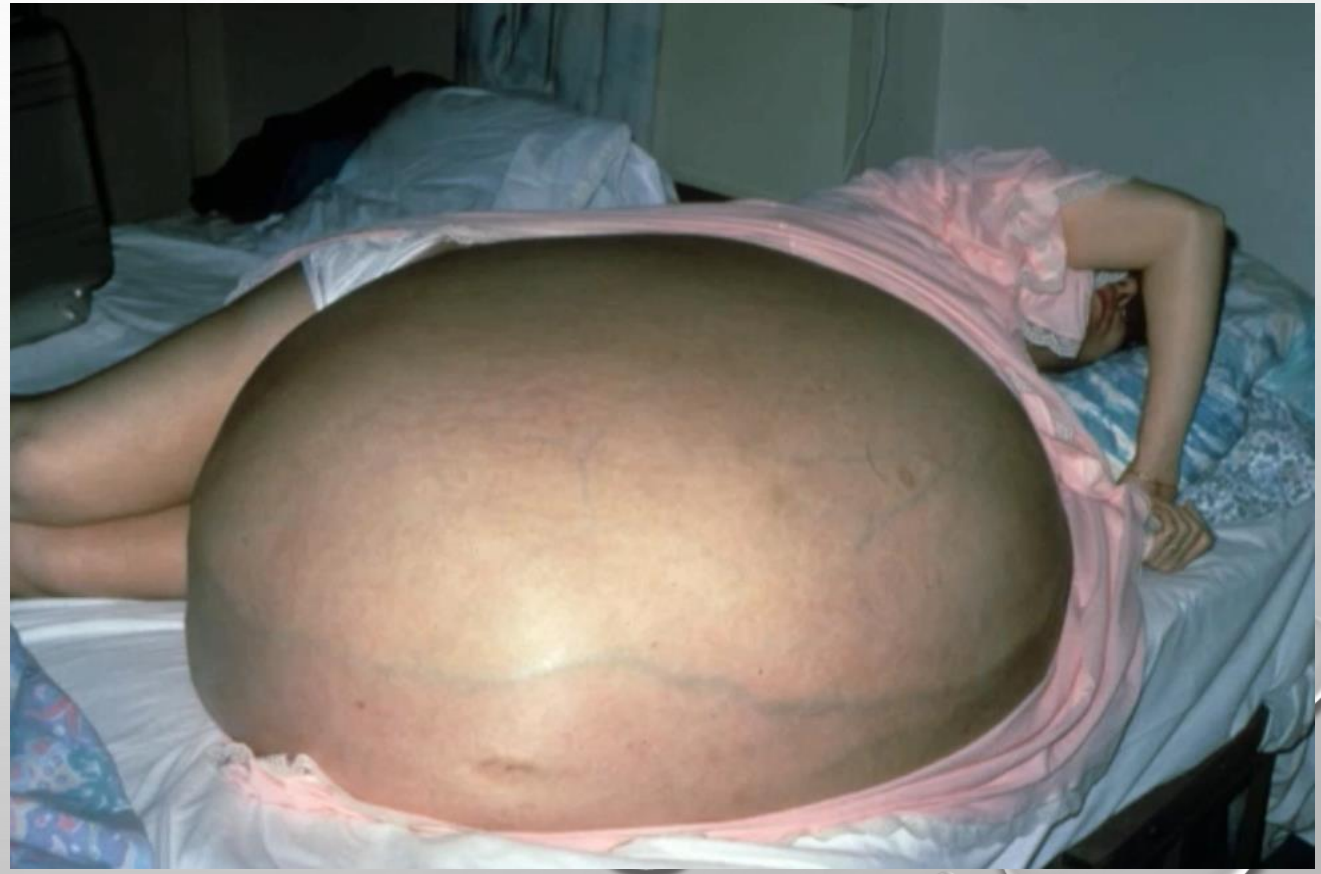
Resection of a 303.2-Pound Ovarian Tumor

KATHERINE A. O'HANLAN, M.D.

Gynecologic Cancer Service, Stanford University School of Medicine, Stanford, California 94305-5317

Received April 8, 1993





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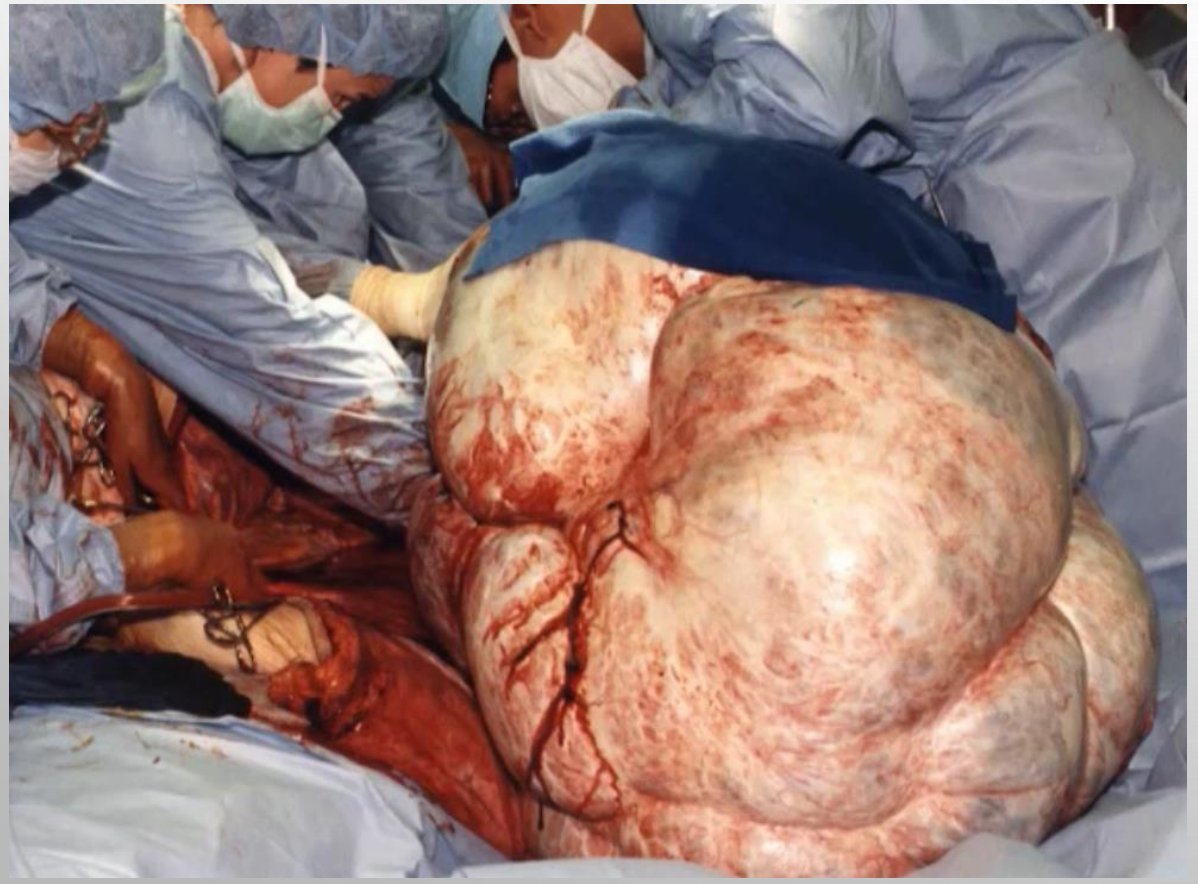
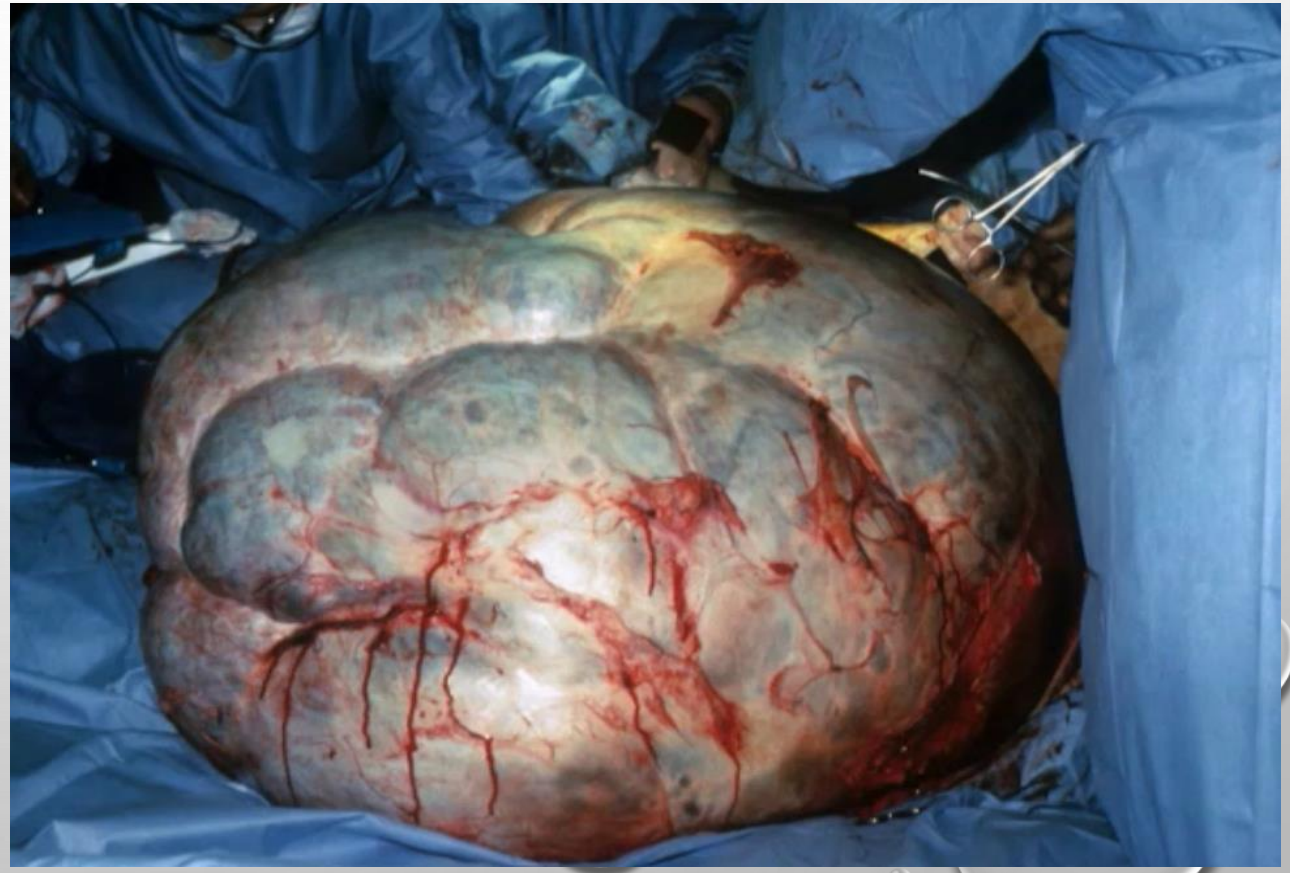




CLINICAL PRESENTATION

- OFTEN PRESENT AS VERY LARGE OVARIAN MASSES WITH SYMPTOMATIC MASS EFFECTS
- INTACT REMOVAL CAN BE CHALLENGING DUE TO ADHESIONS AND EXPOSURE
- THE MAJORITY OF MUCINOUS LESION
  - BENIGN
  - BORDERLINE
  - LOW GRADE MUCINOUS OVARIAN CANCER (TYPE 1 CANCER)
- PRIMARY MUCINOUS OVARIAN CANCER
  - RARE (0.5% TO 1.5% OF ALL OVARIAN CANCERS)
  - OFTEN PRESENT IN PATIENTS 30-50 YO
  - DOES NOT SHARE SIMILAR RISK PROFILE AS SEROUS OVARIAN CANCERS
  - MOST INVASIVE MUCINOUS TUMORS FOUND IN THE OVARY ARE METASTASIS FROM THE GASTROINTESTINAL TRACT (COLON, PANCREAS, AND APPENDIX)

CLINICAL PRESENTATION – PRIMARY OVARIAN MUCINOUS CARCINOMA

- OFTEN CONFINED TO THE OVARY WITHOUT SURFACE INVOLVEMENT
- UNILATERAL (METASTASES ARE BILATERAL)
- SIGNIFICANT SIZE (≥13 CM)
- ELEVATED CEA OR CA19-9

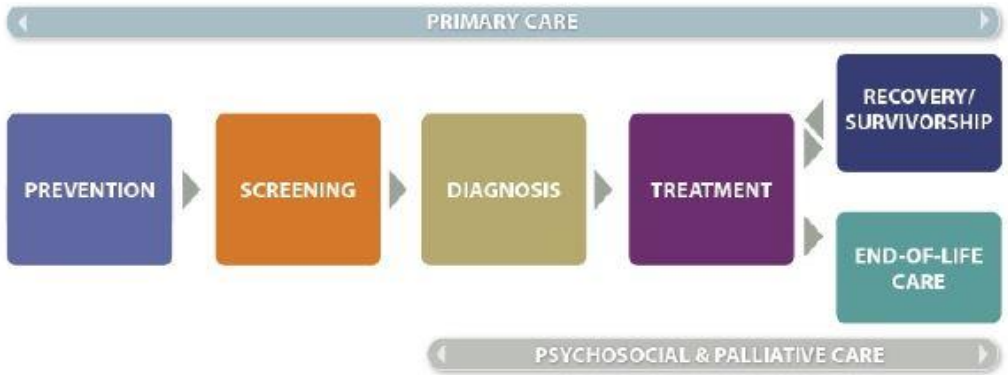
CLINICAL MANAGEMENT

- PERSISTENT LARGE SYMTOMATIC MASSES OFTEN REQUIRE EXPLORATORY SURGERY
  - DIAGNOSIS AND STAGING / DEBULKING AS APPROPRIATE
- DIFFERENTIATING PRIMARY OVARIAN MUCINOUS TUMOUR FROM METASTATIC MUCINOUS TUMOUR OF GASTROINTESTINAL OR OTHER GYNAECOLOGICAL ORIGIN IS CHALLENGING
- THE MAIN PURPOSE OF INTRAOPERATIVE CONSULTATION FOR AN OVARIAN MASS IS TO DETERMINE WHETHER A MALIGNANCY IS PRESENT SO THAT STAGING CAN PROCEED
  - METASTATIC NEOPLASMS TO THE OVARY ARE FREQUENT AND MAY PRESENT PRIOR TO THE DIAGNOSIS OF THE PRIMARY LESION (GASTROINTESTINAL AND HEPATOBILIARY TRACTS AND PANCREAS)
  - NEARLY ALL PRIMARY OVARIAN MUCINOUS CARCINOMAS ARE LARGE AND UNILATERAL
- CONSIDERATION OF APPENDECTOMY IN ALL MUCINOUS OVARIAN TUMOUR

Cancer Care Ontario

Mucinous Epithelial Ovarian Cancer Treatment and Follow-up Pathway Map

Version 2016.10



Disclaimer

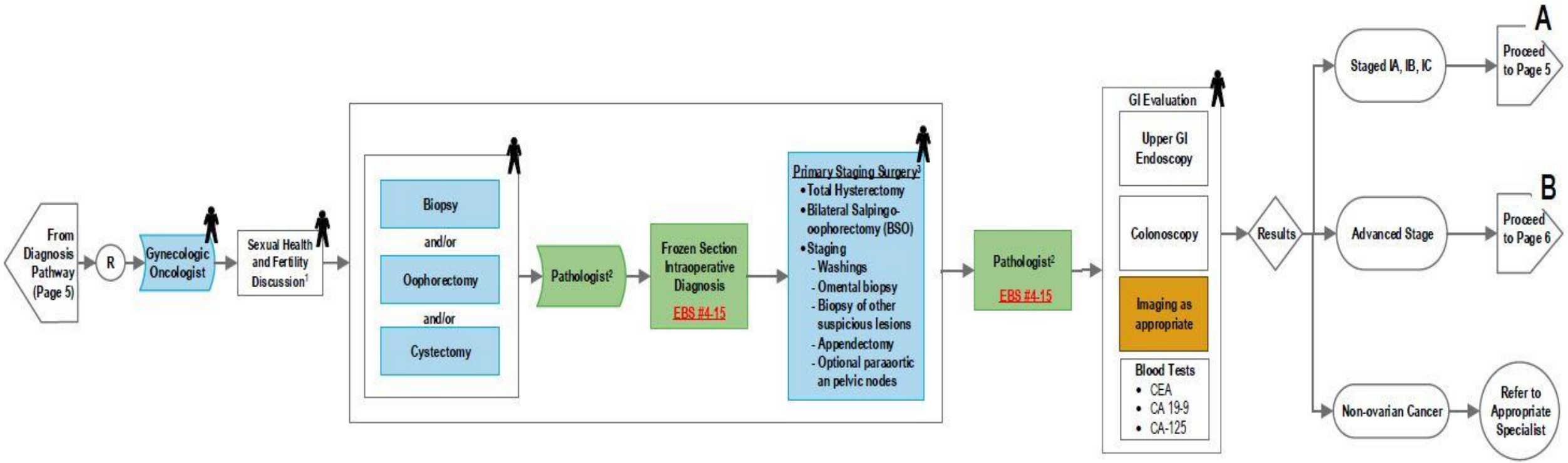
The pathway map is intended to be used for informational purposes only. The pathway map is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. Further, all pathway maps are subject to clinical judgment and actual practice patterns may not follow the proposed steps set out in the pathway map. In the situation where the reader is not a healthcare provider, the reader should always consult a healthcare provider if he/she has any questions regarding the information set out in the pathway map. The information in the pathway map does not create a physician-patient relationship between Cancer Care Ontario (CCO) and the reader.

Ontario
Cancer Care Ontario

Screen for psychosocial needs, and assessment and management of symptoms. Click here for more information about symptom assessment and management tools

Consider the introduction of palliative care, early and across the cancer journey Click here for more information about palliative care

Please note: References to documents that are highlighted in red, bold, underlined font are CCO guidance documents that are currently in development or undergoing review.



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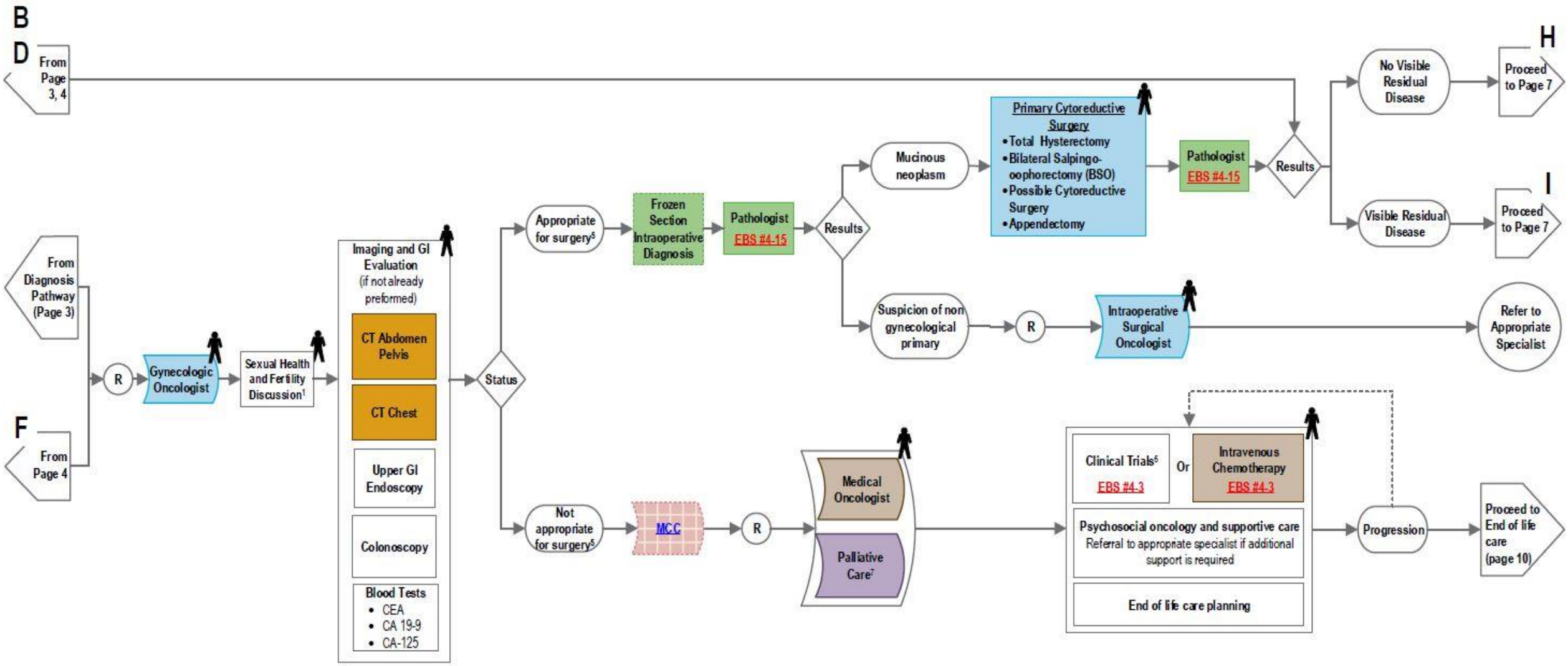

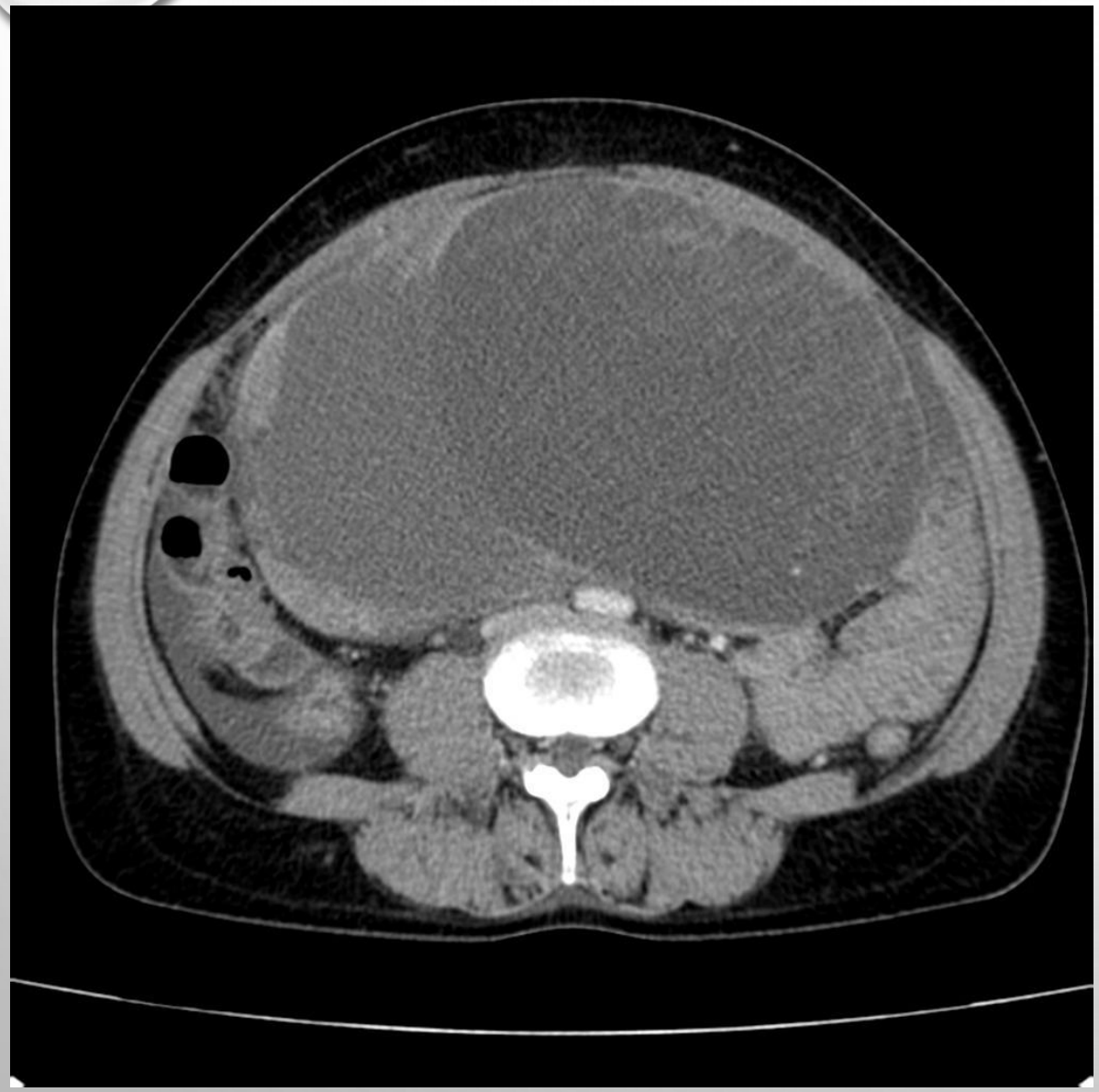

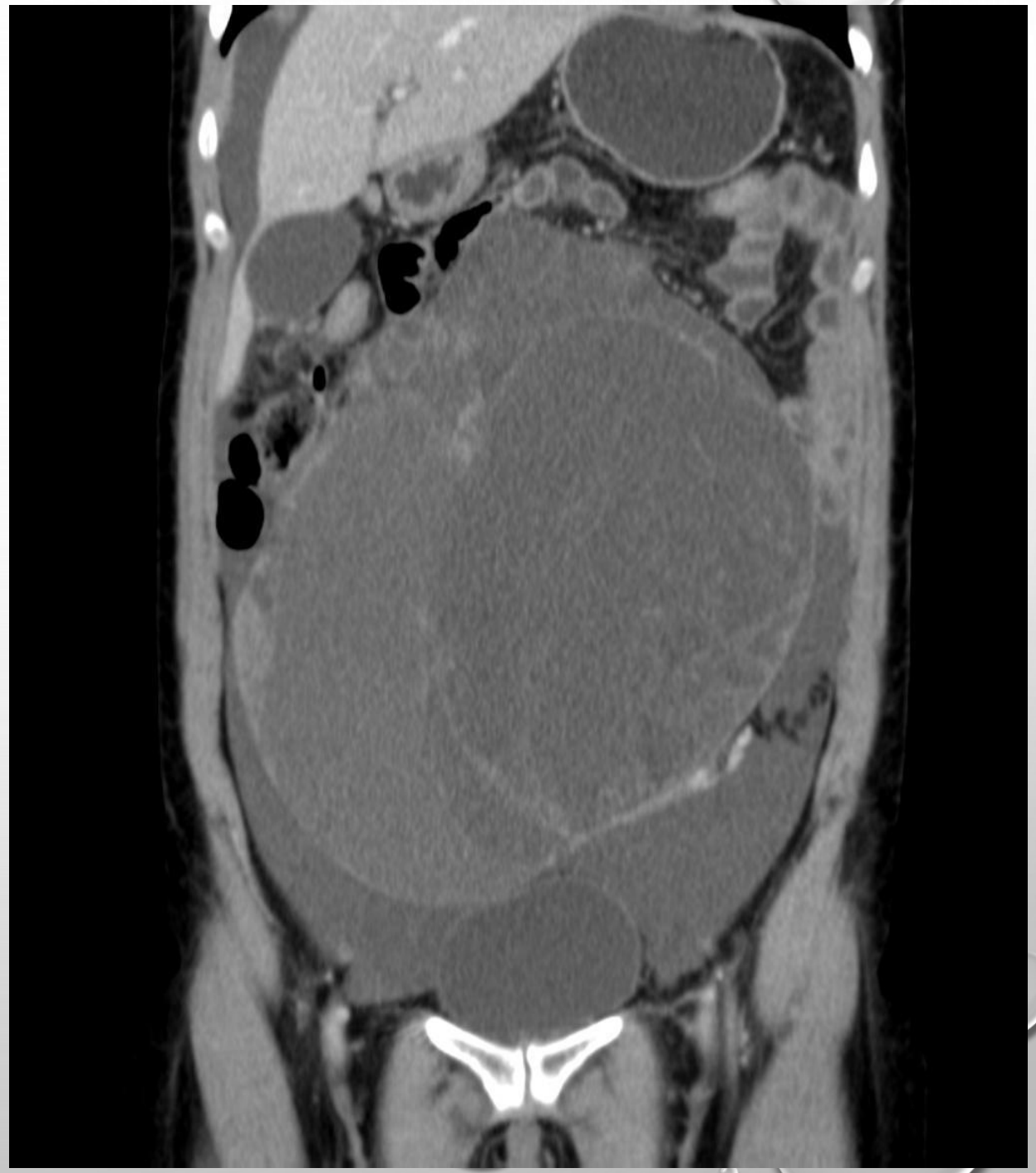

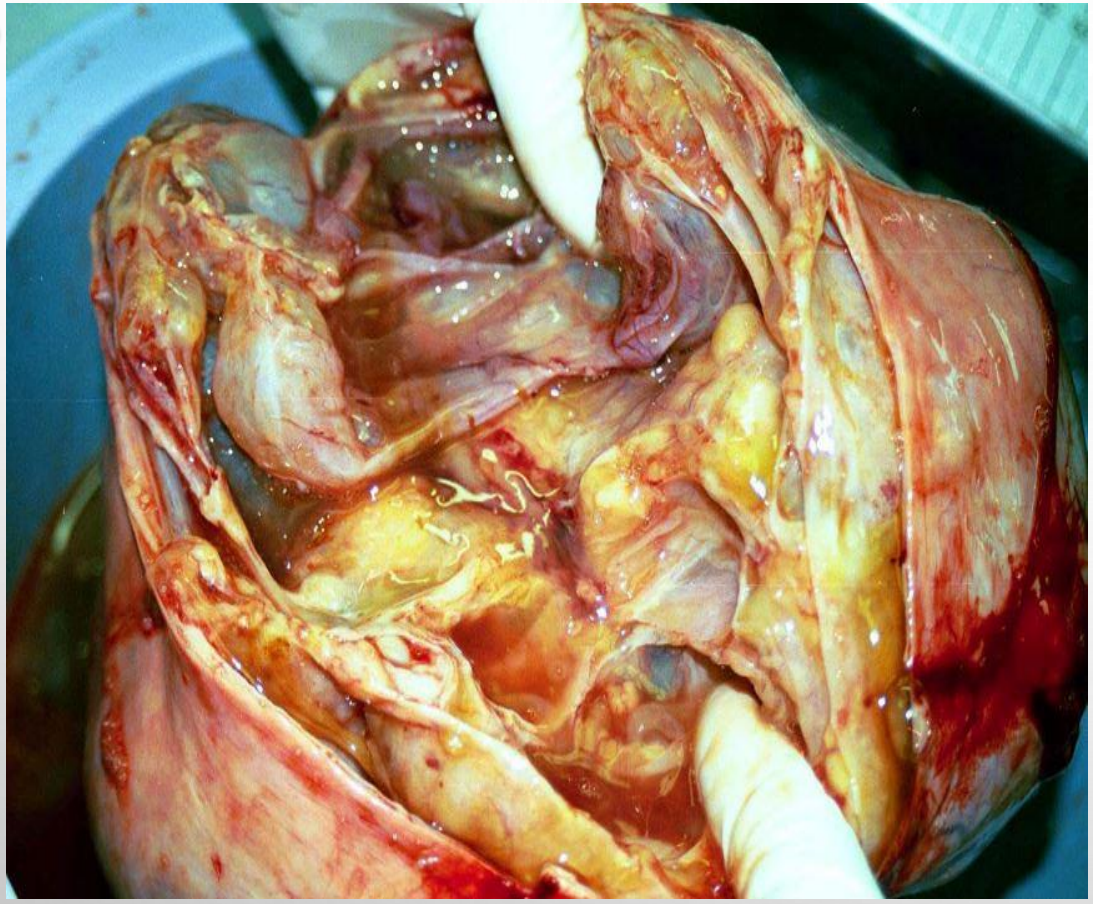

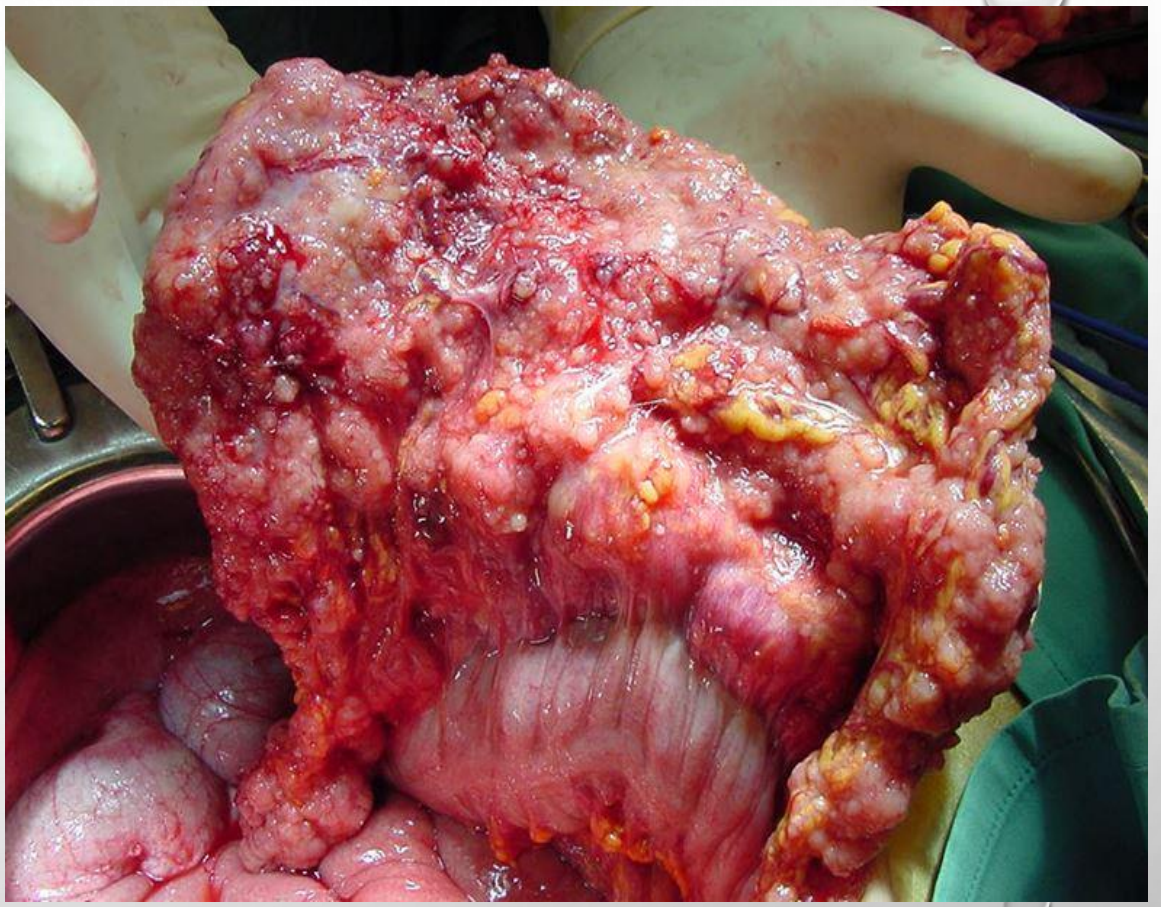

European Journal of Obstetrics & Gynecology and Reproductive Biology 229 (2018) 112–116

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

The role of appendectomy in patients with mucinous borderline ovarian tumors

Taejong Song[a], Min Kyu Kim[b], Yong Wook Jung[c], Bo Seong Yun[c], Seok Ju Seong[c], Chel Hun Choi[d], Tae-Joong Kim[d], Jeong-Won Lee[d], Byoung-Gie Kim[d], Duk-Soo Bae[d,*]

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Table 3
Published studies documenting the frequency of appendectomy, and the incidence of primary and metastatic malignancy of the appendix.

Reference First author, year	mBOT n	Appendectomy performed n (%)	Primary appendiceal mucinous malignancy n (%)	Metastatic appendiceal malignancy n (%)
Fotopoulou, 2009 [18]	12	12 (100%)	0	1 (8.3%)
Timofeev, 2010 [19]	26	26 (100%)	0	0
Koskas, 2011 [20]	97	23 (24%)	0	0
Lin, 2013 [14]	68	41 (60%)	0	0
Feigenberg, 2013 [15]	30	30 (100%)	2 (0.7%)	0
Kleppe, 2014 [21]	98	13 (13%)	0	0
Ozcan, 2015 [22]	69	47 (67%)	0	0
Cosyns, 2016 [23]	27	8 (30%)	0	0
Mukhopadhyay, 2016 [24]	57	40 (70%)	0	0
Present study	473	201 (42%)	1 (0.5%)	1 (0.5%)
Total	957	441 (46%)	3 (0.7%)	2 (0.5%)

Abbreviation. mBOT, mucinous borderline ovarian tumor.

MUCINOUS OVARIAN LESIONS

- CYSTADENOMAS, BORDERLINE , AND CARCINOMAS (INTRAEPITHELIAL AND INVASIVE)
  - DEGREE OF COMPLEXITY , EPITHELIAL PROLIFERATION, PRESENCE OF STROMAL INVASION
  - WIDELY DIFFERENT BIOLOGIC BEHAVIOURS AND PROGNOSIS
- BORDERLINE MUCINOUS OVARIAN TUMOURS
  - GASTROINTESTINAL AND ENDOCERVICAL-LIKE (SEROMUCINOUS TUMORS) TYPE
    - GASTROINTESTINAL TYPES OFTEN HAVE BENIGN BEHAVIOUR
    - SEROMUCINOUS TUMORS ARE MUCH LESS COMMON BUT ALSO HAVE A BENIGN BEHAVIOUR
- BORDERLINE MUCINOUS TUMORS WITH INTRAEPITHELIAL CARCINOMA
  - OFTEN HAVE AN EXCELLENT PROGNOSIS
- BORDERLINE MUCINOUS TUMORS WITH MICROINVASION
  - SMALL (2-5 MM) FOCI OF STROMAL INVASION
  - APPEARS TO ALSO HAVE A GOOD PROGNOSIS

PSEUDOMYXOMA PERITONEII

- MUCOID PERITONEAL NODULES AND/OR MUCINOUS ASCITES ARE ACCOMPANIED BY LOW-GRADE NEOPLASTIC MUCINOUS EPITHELIUM ASSOCIATED WITH POOLS OF EXTRACELLULAR MUCIN
- VIRTUALLY ALL CASES OF PSEUDOMYXOMA PERITONEI ARE DERIVED FROM LOW-GRADE MUCINOUS ADENOMAS, USUALLY OF THE APPENDIX
  - OVARIAN INVOLVEMENT IS SECONDARY
  - NO EFFECTIVE THERAPY
    - ? ROLE OF PERITONECTOMY – HIPEC CHEMOTHERAPY
  - REPEATED OPERATIONS OFTEN REQUIRED TO MANAGE SYMPTOMS

INVASIVE MUCINOUS OVARIAN CANCER

- RARE (~3%) USING CENTRAL PATHOLOGY REVIEW WITH MODERN DIAGNOSTIC CRITERIA AND OFTEN PRESENT AT EARLY STAGE 1 DISEASE
  - LARGE, UNILATERAL, MULTICYSTIC MUCUS-CONTAINING TUMORS WITH SMOOTH WHITE CAPSULES
  - OFTEN WELL DIFFERENTIATED ARISING IN AREAS OF BORDERLINE CHANGES (INTESTINAL TYPE)
  - DESTRUCTIVE STROMAL INVASION WITH “CONFLUENT GLANDULAR” OR “EXPANSILE” PATTERN OF INVASION
  - SEROMUCINOUS (MULLERIAN OR ENDOCERVICAL-LIKE) TYPES ARE UNCOMMON
    - DESTRUCTIVE STROMAL INVASION WITH ASSOCIATION WITH ENDOMETRIOSIS
- METASTATIC MUCINOUS CARCINOMAS
  - BILATERAL, SMALLER SIZE (<10 CM TO 12 CM), OVARIAN SURFACE INVOLVEMENT, A NODULAR PATTERN OF OVARIAN INVOLVEMENT AND HAPHAZARD PATTERN OF INFILTRATIVE MUCINOUS GLANDS IRREGULARLY DISTRIBUTED THROUGHOUT THE OVARIAN STROMA, VASCULAR INVASION
  - DIFFERENTIAL IMMUNOHISTOCHEMICAL PATTERNS (CK7 , CK 20, HPV AND P16, MAMMAGLOBIN AND GCDFP-15, DPC4
  - MOLECULAR PROFILING :KRAS (40%-50%), HER2 AMPLIFICATION (19%) - ? BETTER PROGNOSIS

METASTATIC MUCINOUS OVARIAN CANCER

SEDMAN ET AL (THE AMERICAN JOURNAL OF SURGICAL PATHOLOGY *27(7): 985-993, 2003)*

- 52 MUCINOUS ADENOCARCINOMAS INVOLVING THE OVARIES
  - 23% PRIMARY OVARIAN NEOPLASMS AND 77% WERE METASTATIC TUMORS
  - 45% GASTROINTESTINAL TRACT, 20% PANCREATIC , 5% ENDOMETRIAL, 13% CERVICAL , 8% BREAST , 10% UNKNOWN PRIMARY SITE
  - EXTRAOVARIAN PELVIC AND ABDOMINAL PERITONEAL IN ALL PATIENTS WITH GI CARCINOMAS AND IN APPROXIMATELY HALF OF THOSE WITH NONGASTROINTESTINAL CARCINOMAS

ARTICLE IN PRESS

YGYNO-977133; No. of pages: 9; 4C: 4, 5, 6

Gynecologic Oncology xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Massively parallel sequencing analysis of mucinous ovarian carcinomas: genomic profiling and differential diagnoses

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ARTICLE INFO

Article history:
Received 1 March 2018
Received in revised form 30 April 2018
Accepted 7 May 2018
Available online xxxx

Keywords:
Mucinous ovarian cancer
Massively parallel sequencing
Immunohistochemistry
Classification
Diagnosis

ABSTRACT

Objective. Mucinous ovarian cancer (MOC) is a rare type of epithelial ovarian cancer resistant to standard chemotherapy regimens. We sought to characterize the repertoire of somatic mutations in MOCs and to define the contribution of massively parallel sequencing to the classification of tumors diagnosed as primary MOCs.

Methods. Following gynecologic pathology and chart review, DNA samples obtained from primary MOCs and matched normal tissues/blood were subjected to whole-exome ($n = 9$) or massively parallel sequencing targeting 341 cancer genes ($n = 15$). Immunohistochemical analysis of estrogen receptor, progesterone receptor, PTEN, ARID1A/BAF250a, and the DNA mismatch (MMR) proteins MSH6 and PMS2 was performed for all cases. Mutational frequencies of MOCs were compared to those of high-grade serous ovarian cancers (HGSOCs) and mucinous tumors from other sites.

Results. MOCs were heterogeneous at the genetic level, frequently harboring *TP53* (75%) mutations, *KRAS* (71%) mutations and/or *CDKN2A/B* homozygous deletions/mutations (33%). Although established criteria for diagnosis were employed, four cases harbored mutational and immunohistochemical profiles similar to those of endometrioid carcinomas, and one case for colorectal or endometrioid carcinoma. Significant differences in the frequencies of *KRAS*, *TP53*, *CDKN2A*, *FBXW7*, *PIK3CA* and/or *APC* mutations between the confirmed primary MOCs ($n = 19$) and HGSOCs, mucinous gastric and/or mucinous colorectal carcinomas were found, whereas no differences in the 341 genes studied between MOCs and mucinous pancreatic carcinomas were identified.

Conclusions. Our findings suggest that the assessment of mutations affecting *TP53*, *KRAS*, *PIK3CA*, *ARID1A* and *POLE*, and DNA MMR protein expression may be used to further aid the diagnosis and treatment decision-making of primary MOC.

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Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Does the primary site really matter? Profiling mucinous ovarian cancers of uncertain primary origin (MO-CUP) to personalise treatment and inform the design of clinical trials

Nicola S. Meagher [a,b,*], Klaus Schuster [c], Andreas Voss [c], Timothy Budden [a], Chi Nam Ignatius Pang [d], Anna deFazio [e], Susan J. Ramus [a,f], Michael L. Friedlander [b,g]

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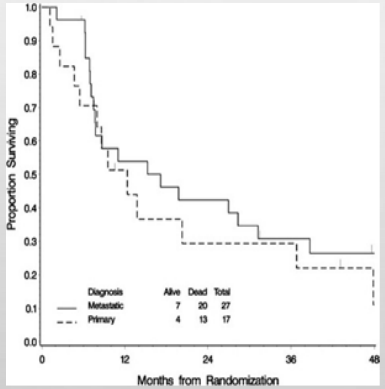
HIGHLIGHTS

- Advanced mucinous ovarian cancers are rare with few histotype specific trials.
- Includes mucinous ovarian cancers of uncertain primary (MOCUP).
- Tumor profiling MOCUPs to identify treatment targets for basket trials needed.
- Largest reported series of MOCUPS and includes almost 300 invasive cancers.
- Most common mutations were *KRAS* (60%), *TP53* (38%), *PIK3CA* (13%) and *PTEN* (9%).

INVASIVE MUCINOUS OVARIAN CANCER – CLINICAL BEHAVIOURS

- STAGE I MUCINOUS CARCINOMAS HAVE A SURVIVAL OF ABOUT 90%
- ADVANCED STAGE HAS MUCH WORSE PROGNOSIS THAN SEROUS TYPES
  - POOR RESPONSE TO STANDARD SYSTEMIC CHEMOTHERAPY
    - MEDIAN DISEASE FREE SURVIVAL FOR WOMEN WITH STAGE III/IV MUCINOUS TUMORS 14.6 MONTHS VS 42 MONTHS FOR SEROUS SUBTYPE (ZAINO ET AL. CANCER. 2011;117(3):554-62)
    - PRIMARY VS METASTATIC



  - POORLY REPRESENTED IN OVARIAN CANCER RCT (3-7%)

INVASIVE MUCINOUS OVARIAN CANCER – CLINICAL BEHAVIOURS

HESS V, A'HERN R, NASIRI N ET AL. MUCINOUS EPITHELIAL OVARIAN CANCER: A SEPARATE ENTITY REQUIRING SPECIFIC TREATMENT. J CLIN ONCOL 2004; 22: 1040-1044

- THE RESPONSE RATE TO PLATINUM-BASED THERAPY WAS 26% VS 65% (MUCINOUS VS NON MUCINOUS)
- THE MEDIAN PROGRESSION-FREE SURVIVAL AND OS WERE 5.7 VERSUS 14.1 MONTHS AND 12 VERSUS 16.7 MONTHS (MUCINOUS VS NON MUCINOUS)

MUCINOUS OVARIAN CANCER – PROSPECTIVE CLINICAL TRIAL

- GOG241 INVESTIGATES THE UTILITY OF CHEMOTHERAPY AGENTS FOR GI CANCER (OXALIPLATIN + CAPECITABINE VS CARBOPLATIN + PACLITAXEL WITH/WITHOUT AVASTIN)
  - PREMATURE CLOSURE: ONLY 50 OF A PROPOSED 322 PATIENTS RECRUITED
  - ONLY SEVENTEEN WERE CONFIRMED TO HAVE MUCINOUS PRIMARY (34%)
  - RESPONSES : 4 OF 26 (15.4%) IN THE OXALIPLATIN/CAPECITABINE ARMS VS 6 OF 24 (25%) IN THE CARBOPLATIN/PACLITAXEL ARMS
  - PFS FOR THE OXALIPLATIN/CAPECITABINE ARMS WAS 10.1MTHS VS. 15.4 MTHS FOR THE CARBOPLATIN/PACLITAXEL ARMS (HR 1.08; 95% CI 0.53-2.19; P = 0.83)
  - THE MEDIAN PFS IN ARMS WITH BEVACIZUMAB WAS 17.4MTHS VS. 8.8MTHS IN ARMS WITHOUT BEVACIZUMAB (HR 0.88; 95% CI 0.43-1.79; P=0.72)
- TREAT BASED ON MOLECULAR PROFILING (SITE AGNOSTIC STRATEGY)
  - HER2 (TRASTUZUMAB) , KRAS (CETUXIMAB), PD1/PD-L1
  - SRC KINASE , DUAL PI3K AND MTOR INHIBITORS

CONCLUSION

- WIDE SPECTRUM OF MUCINOUS OVARIAN LESIONS ENCOUNTERED IN CLINICAL PRACTICE
- PRIMARY OVARIAN MUCINOUS CANCER IS RARE – MOST OFTEN METASTATIC INVOLVEMENT FROM OTHER SITES
- MOST PRIMARY OVARIAN MUCINOUS LESION PRESENT AT AN EARLY SURGICAL STAGE WITH GOOD PROGNOSIS
- METASTATIC MUCINOUS OVARIAN CANCER HAS A POOR PROGNOSIS DUE TO MAINLY LOWER CHEMOTHERAPY RESPONSE COMPARED TO SEROUS
- VERY DIFFERENT BIOLOGIC BEHAVIOURS FROM OTHER HISTOLOGIES