Molecular Pathological Phenotypes and Outcome in Adenocarcinoma of the Ampulla of Vater

*Personalised Medicine*
“Selecting the right treatment, for the right patient, at the right time”

Andrew Biankin
Garvan Institute of Medical Research, Sydney, Australia
Ampullary Cancer

- 2nd most common after PDAC
- 6-20% of Whipple’s
- **Broad range of outcomes**
- Ca may arise from:
  - Duodenal
  - Biliary
  - Pancreatic origin
- Adj chemo - no survival benefit (RCT & cohort study)
- ? heterogeneity
- ? different phenotypes
Key Clinical Questions

• Patient selection for surgical treatment
  ▪ Who to operate on?
  ▪ How aggressive?
  ▪ Ampullectomy or resection?

• Patient selection for adjuvant chemotherapy
  ▪ Is it necessary?
  ▪ Which type of chemotherapy?

• How do we interpret and design clinical trials?
  (eg. ESPAC-3, 5-FU Vs GEM)
Aim

- To define clinically and biologically relevant phenotypes of prognosis and therapeutic responsiveness with potential clinical utility

Methods

- N = 72 (NSWPCN)
- TMA
- IHC (CDX2 and MUC1) + MUC2, CK7, CK20
Intestinal Vs Pancreaticobiliary
A. HISTOLOGICAL SUBTYPE

$P = 0.0169$
Median Survival 115.5 Vs 22.0 months
n = 72

B. MOLECULAR PATHOLOGICAL PHENOTYPE

$P = 0.0002$
Median Survival 115.5 Vs 16.1 months
n = 72

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3 Distinct Prognostic Phenotypes

- Prognosticate
- Chemotherapy
  - Yes / No
  - Which one?
- Previous trial interpretation
- Future trial design

### Models

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<th>Models</th>
<th>Variable</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-Value</th>
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<tr>
<td>D. Ampullary Cancer</td>
<td>Lymph Node Metastases (Positive)</td>
<td>3.19 (1.54 – 6.58)</td>
<td>0.0017</td>
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<td>(n = 72)</td>
<td>Molecular Pathological Phenotype (PB)</td>
<td>3.40 (1.71 – 6.76)</td>
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**INTESTINAL SUBTYPE & CDX2 POSITIVE**

- **CUMULATIVE SURVIVAL**
- **P = 0.0001**
  - Median Survival 172.8 Vs 36.2 months
- **At Risk**
  - LN NEG: 13, 13, 11, 7, 6, 5, 4, 4, 3
  - LN POS: 7, 6, 2, 1, 1, 0
- **MONTHS**

**Cancer Research Program**
Conclusions

• Ampullary Ca is heterogeneous with a broad range of outcomes

• 3 distinct phenotypes:
  ▪ Better patient selection for surgery and chemotherapy
  ▪ Interpret previous clinical trials
  ▪ Stratification for future trials
  ▪ Prospective validation encouraged
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