Factor V inhibitors

- **Alloantibodies due to Factor V deficiency**
  - FV def: 1/ million in caucasians. Ten times more common in Iran and Southern India
  - Approximately 2% of all FV inhibitors reported.
  - Usually post FFP therapy

- **Spontaneous auto-antibodies**
  - **Antibiotics** (42%) Beta-lactams aminoglycosides (streptomycin), cephalosporins, tetracyclines and
    chinolones (ciprofloxacin)
  - **Surgical procedures** (31%): cardiovascular (55.5%), abdominal (37.1%), neurosurgery (7.1%)
  - **Infections** (23%) - Bacterial and Viral (HCV, HBV, HIV)
  - **Malignancy** (22%) - Mainly solid tumours
  - **Autoimmune conditions** (13%)
  - **Pregnancy**

- **Cross-reacting anti-bovine factor V antibodies – Fibrin/thrombin glues**
  - Post-topical bovine thrombin exposure once a common event.
  - association with other antibodies due to contamination with FV and other proteins
  - Less frequent now with use of human and recombinant thrombin in preparations (e.g. Tisseel, Evithrom®,
    Recombithrom®)

Factor V inhibitors

• Rare
• Incidence
  – Singapore – 0.09 cases per million.
  – Australia – 0.29 cases per million.
• Most haemostasis referral labs will see one case every five years or so.
Bleeding

• Bleeding present in 81% of cases
  – 32% multiple sites simultaneously
  – 62% mucous membranes (i.e., gastrointestinal, genitourinary (often severe) and airway tracts)
  – 16% post surgical procedures related to site.
  – 8% Intracranial haemorrhage - highest mortality rate (50%).

• 4 cases with thrombotic complications
• Inhibitor level is not predictive of bleeding risk (not surprising given survey results though!)
Outcome

• Death 14%
• Disappearance 69% (of which 22% spontaneous)
• Median time to remission 6 weeks (1 week to 29 months).
• Prognosis strictly related to underlying “cause”
  – BEST
    • antibiotic-associated (79% rem, 6% death)
    • idiopathic (75% rem, 0% death)
  – WORST
    • Autoimmune disorders (60% rem, 30% death)
    • cancers (64% rem, 24% death) the worst. Obvious confounders here!
FV inhibitors

• Should be suspected in any acquired post–op coagulopathy.
• Unexplained haematuria
• Any unexplained elevation of PT and APTT really!
• Confirmation of use of bovine thrombin can be difficult. Review of ALL records often necessary (ie surgical, anaesthetic etc) as its use is often poorly documented.
Diagnosis of FV inhibitors

- Prolonged PT and APTT
- Not fully correctable on 1:1 mixing studies
- Low level of FV demonstrated
- Inhibitor specificity to FV demonstrated.
- Usually complete inactivation of FV within 15 minutes (cf FVIII inhibitors).
- Full 2 hours incubations performed to accurately quantify with the Bethesda method.
Treatment

1. Control the bleeding
2. Eradicate the Antibody
3. Remove the trigger factor

NO EVIDENCE BASED TREATMENT

• Asymptomatic
  – Not necessary

• Symptomatic
  – Replacement therapy for bleeding control
    • Platelets – used in 22% of cases with 71% success
    • rFVII 4 cases.
    • FFP, PCC – very variable.
  – Plasmapheresis, immunoadsorption
  – Immunosuppression (63% of cases, 76% success rate)
    • Corticosteroids
    • Cyclophosphamide
    • Rituximab

• Combination of A, B and C probably most effective
• IVlg used with inconsistent results
HAEMATOLOGY

Mis-identification of factor inhibitors by diagnostic haemostasis laboratories: recognition of pitfalls and elucidation of strategies. A follow up to a large multicentre evaluation

EMMANUEL J. FAVALORO, ROSLYN BONAR, ELIZABETH DUNCAN, GAIL EARL, JOYCE LOW, MARGARET ABOUD, SARAH JUST, JOHN SIOUFI, ALISON STREET, KATHERINE MARSDEN (ON BEHALF OF THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA QUALITY ASSURANCE PROGRAM IN HAEMATOLOGY HAEMOSTASIS COMMITTEE)

Department of Haematology and Royal College of Pathologists of Australasia Quality Assurance Program (RCPA QAP), Institute of Clinical Pathology and Medical Research (ICPMR), Westmead Hospital, New South Wales, Australia

-RCPA QAP- 2006
-42 labs
-8 samples for evaluation.
-Mixture of true high FV inhibitor, moderate FVIII inhibitor, true LAC, normal slightly aged plasma, normal serum sample, normal EDTA, oral AC, gross heparin sample.
## Summary of findings

<table>
<thead>
<tr>
<th>Sample/specimen type</th>
<th>% correct responses</th>
<th>Key incorrect responses (false pos/false neg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal EDTA plasma</td>
<td>2.4</td>
<td>68.3% identified FV +/- FVIII inhibitors.</td>
</tr>
<tr>
<td>Strong FV inhibitor -citrate plasma</td>
<td>63.4</td>
<td>4.8% identified FVIII inhib. 17.1% identified LA only, 14.6% identified FV+/− FVIII deficiency.</td>
</tr>
<tr>
<td>Normal plasma, heparin anticoagulant</td>
<td>68.3</td>
<td>22.0% identified specific factor inhibitor (FV, FVIII, FXI)</td>
</tr>
<tr>
<td>Normal (aged) plasma/citrate sample</td>
<td>87.8</td>
<td>4.8% identified a possible inhibitor, 4.9% LA, 2.4% heparin contamination.</td>
</tr>
<tr>
<td>FVIII inhibitor/ plasma defibrinogenated by heat treatment</td>
<td>46.3</td>
<td>53.6 % identified some other sample issue (serum, snake bite) and no further investigation for inhibitor.</td>
</tr>
<tr>
<td>Normal serum/ plasma defibrinogenated by clotting</td>
<td>90.2</td>
<td>4.9% identified a factor deficiency. 4.9% identified an inhibitor.</td>
</tr>
<tr>
<td>LA/citrate plasma</td>
<td>97.6</td>
<td>2.4% identified FVIII deficiency.</td>
</tr>
<tr>
<td>Absorbed plasma ('warfarin/vitamin K deficiency/liver disease')/ citrate plasma</td>
<td>92.7</td>
<td>7.3% identified a specific factor deficiency.</td>
</tr>
</tbody>
</table>
Summary of survey findings

- Level of inhibitor varied widely. Actual FV inhibitor level >250BU.
- 10-250BU reported with most labs in 16-40BU range
**27/05/09** | **01/07/09**
---|---
FII (U/ml) | 0.78 | 0.77
FV | 0.04 | 0.27
FVII | 0.57 | 0.86
FVIIIc | 1.44 |  | 
FIX | 0.90 | 1.03
FX | 0.66 | 0.66
FXI | 0.73 |  | 
FXII | 0.69 |  | 
PT (10-14s) | 35 | 31
APTT (24-40s) | 80 | 44
Inhibitor level | 5.9BU | None detected

No treatment as no bleeding.
Take home points

- FV inhibitors are rare
- Index of clinical suspicion should be high in post-surgical patients with evolving coagulopathy.
- Standard laboratory assays do not reliably predict bleeding risk.
- Treatment is guided by the severity of symptoms. A combination of replacement therapy (platelets), plasmapheresis and immunosuppression probably the most effective.
- In the event of an acute bleed, there is no evidence-based recommendations.
Case 4

Clinical details

• 43 year old male
• “Macrocytic anaemia ? cause”

<table>
<thead>
<tr>
<th></th>
<th>Full blood count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>97</td>
</tr>
<tr>
<td>MCV</td>
<td>104</td>
</tr>
<tr>
<td>WCC</td>
<td>4.9</td>
</tr>
<tr>
<td>PLT</td>
<td>169</td>
</tr>
<tr>
<td>Neuts</td>
<td>2.7</td>
</tr>
<tr>
<td>Lymphs</td>
<td>1.9</td>
</tr>
<tr>
<td>Monos</td>
<td>0.2</td>
</tr>
<tr>
<td>Eos</td>
<td>0.04</td>
</tr>
<tr>
<td>Basos</td>
<td>0.07</td>
</tr>
</tbody>
</table>

135-180 g/l
80-100 fl
4.0-11.0
150-400
2.0-7.5
1.2-4.0
0.2-1.0
0-0.5
0-0.2
Blood film
BM aspirate

Myelogram:
Blasts: 0%
Pros: 8%
Myelos: 1%
Metas: 1%
Neuts: 26%
Eryth: 59%
Lymphs: 3%
Monos: 0%
Plasma: 0%
Eos: 0%
Basos: 0%
M:E 0.64
Trephine

Erythroid hyperplasia
Perl’s Stain

**Iron studies**
- Ferritin: 5490
- Iron: 39
- Transferrin: 21
- TSAT: 93%
Diagnosis?

Congenital dyserythropoietic anaemia type I (CDA-I).

Other investigations?
"Sponge-like" or "Swiss cheese" nuclei.
NM_138477.2(CDAN1):c.156C>G

Codanin 1: Role in nuclear envelope integrity, possibly related to microtubule attachments.
500 nRBC examined.
≥ 1% bridged
<10 binucleate

<table>
<thead>
<tr>
<th>CDA type</th>
<th>CDA type II</th>
<th>CDA type III familial</th>
<th>CDA type III sporadic</th>
<th>CDA variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inheritance</td>
<td>Autosomal recessive</td>
<td>Autosomal recessive</td>
<td>Dominant</td>
<td>Variable</td>
</tr>
<tr>
<td>Cases reported</td>
<td>&gt;300</td>
<td>&gt;450</td>
<td>2 families</td>
<td>&lt;20</td>
</tr>
<tr>
<td>BM morphology (light microscopy)</td>
<td>Abnormal chromatin structure, chromatin bridges</td>
<td>Binularity, multinuclearity of mature erythroblasts</td>
<td>Giant multinucleated erythroblasts</td>
<td>Giant multinucleated erythroblasts</td>
</tr>
<tr>
<td>BM EM findings</td>
<td>“Spongy” heterochromatin, invagination of cytoplasm into the nucleus</td>
<td>Peripheral cysterna beneath the plasma membrane</td>
<td>Clefts in heterochromatin, autophagic vacuoles, intranuclear cisternae</td>
<td>Various</td>
</tr>
<tr>
<td>Mutated gene</td>
<td>CDAN1, C15orf41</td>
<td>SEC23B</td>
<td>KIF23</td>
<td>Unknown</td>
</tr>
<tr>
<td>Associated dysmorphology/organ involvement</td>
<td>Skeleton</td>
<td>Variable, rare</td>
<td>Monoclonal gammopathy, myeloma, angiod streaks</td>
<td>Variable</td>
</tr>
</tbody>
</table>


**Congenital dyserythropoietic anemias: molecular insights and diagnostic approach**

Achille Iolascon,1,2 Hermann Heimpel,3 Anders Wahlin,4 and Hannah Tamary5,6

BLOOD, 26 SEPTEMBER 2013 · VOLUME 122, NUMBER 13
Take home points

• You don’t need fancy tests to make theses diagnoses. Just need to look well and know about these conditions.

• Another “paediatric” diagnosis?
Case 5

Clinical details

- 68 yo r female
- 5 week history of fevers. Hepatomegaly, cytopenias ? cause”
- Metastatic uveal melanoma
- Epilimumab and nivolumab therapy
- Hypothyroidism and pernicious anaemia.
- Ferritin 120 000
- Triglycerides 2.2

Full blood count

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Hb</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>MCV</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td>RCC</td>
<td>3.24</td>
</tr>
<tr>
<td></td>
<td>HCT</td>
<td>0.24</td>
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<tr>
<td></td>
<td>WCC</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>PLT</td>
<td>83</td>
</tr>
<tr>
<td>Neuts</td>
<td>3.0</td>
<td>2.0-7.5</td>
</tr>
<tr>
<td>Lymphs</td>
<td>0.7</td>
<td>1.2-4.0</td>
</tr>
<tr>
<td>Monos</td>
<td>0.3</td>
<td>0.2-1.0</td>
</tr>
<tr>
<td>Eos</td>
<td>0.0</td>
<td>0-0.5</td>
</tr>
<tr>
<td>Baso</td>
<td>0.0</td>
<td>0-0.2</td>
</tr>
</tbody>
</table>
Blood film

Toxic features
BM aspirate

Myelogram:
Blasts: 2%
Pros: 18%
Myelos: 5%
Metas: 5%
Neuts: 40%
Eryth: 1%
Lymphs: 23%
Monos: 2%
Plasma: 2%
Eos: 3%
Basos: 0%
M:E: 74.0
Is there melanoma in here?

Histopathology 1997, 31, 367–373

Erythrophagocytic tumour cells in melanoma and squamous cell carcinoma of the skin

C. Monteagudo, E. Jordà*, C. Carca, C. Illueca, A. Peydró & A. Llombart-Bosch
Departments of Pathology and Medicine, and *Dermatology, University Hospital, University of Valencia, Spain

CD68+ Scavenger Receptor Class D
Trephine

No melanoma (S-100, Melan-A)
HLH and pure red cell aplasia secondary to Ipilimumab and Nivolumab therapy
Severe hemophagocytic lymphohistiocytosis in a melanoma patient treated with ipilimumab + nivolumab

Andrew Hantel¹, Brooke Gabster², Jason X. Cheng³, Harvey Golomb¹ and Thomas F. Gajewski¹*  


A case of pure red cell aplasia during nivolumab therapy for cardiac metastatic melanoma

Akihiko Yuki¹, Tatsuya Takenouchi¹, Sumiko Takatsuka¹ and Takuro Ishiguro¹  

Melanoma Research 2017, 27:635–637
Immune check points

• Control excessive immune activation
  – Cytotoxic T lymphocyte antigen 4 (CTLA4) down modulates T-cell activation at time of initial response to antigen.
  – Programmed cell death-1 protein and its ligands (PD1/PDL1) pathway regulates inflammatory responses in tissues by effector T cells. FAS mediated.

• Mechanism by which tumours evade the immune system.
  • Ipilimumab
    – CTLA-4 blockade
  • Nivolumab
    – (PD-1) / PDL1 blockade.
The Nobel Prize in Physiology or Medicine 2018 was awarded jointly to James P. Allison and Tasuku Honjo "for their discovery of cancer therapy by inhibition of negative immune regulation."

Allison plays harmonica in a blues band called “the checkpoints....”
<table>
<thead>
<tr>
<th>Drug name</th>
<th>Target</th>
<th>Date approved</th>
<th>Total(s) based on</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ipilimumab (Yervoy®)</td>
<td>CTLA-4</td>
<td>3/25/2011</td>
<td>NCT0094653</td>
<td>Unresectable or metastatic melanoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10/28/2015</td>
<td>R08C, 18071</td>
<td>Adjunctive treatment for cutaneous melanoma with pathologic involvement of regional LN of &gt; 1 mm following complete resection, including total lymphadenectomy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7/24/2017</td>
<td>NCT01454379, NCT01696045</td>
<td>Expanded approval for unresectable or metastatic melanoma in pediatric patients ≥ 12 years of age</td>
</tr>
<tr>
<td>Nivolumab (Opdivo®)</td>
<td>PD-1</td>
<td>12/2/2014</td>
<td>CheckMate-037 (NCT01721746)</td>
<td>Unresectable or metastatic melanoma that has progressed following treatment with ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3/4/2015</td>
<td>CheckMate-017 (NCT021642004)</td>
<td>Metastatic squamous NSCLC that has progressed on/after platinum-based chemotherapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10/9/2015</td>
<td>CheckMate-057 (NCT01673887)</td>
<td>Non-squamous NSCLC that has progressed on/after platinum-based chemotherapy; patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for those aberrations</td>
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<tr>
<td></td>
<td></td>
<td>11/23/2015</td>
<td>CheckMate-025 (NCT02688794)</td>
<td>Advanced RCC following prior treatment with anti-angiogenic therapy</td>
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<tr>
<td></td>
<td></td>
<td>11/24/2015</td>
<td>CheckMate-006 (NCT02727722)</td>
<td>Unresectable or metastatic BRAF V600 wild-type melanoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5/17/16</td>
<td>CheckMate-039 (NCT01592570), CheckMate-205 (NCT02181738)</td>
<td>Classical Hodgkin lymphoma that has relapsed or progressed after autologous hematopoietic stem cell transplantation and post-transplantation hematimyal vedotin (Adcetris)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11/10/2016</td>
<td>CheckMate-141 (NCT02010438)</td>
<td>Recurrent or metastatic SCLH that has progressed on/after a platinum-based therapy</td>
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<tr>
<td></td>
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<td>2/2/17</td>
<td>CheckMate-275 (NCT02387996)</td>
<td>Locally advanced or metastatic urothelial carcinoma that has progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing chemotherapy</td>
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<tr>
<td></td>
<td></td>
<td>8/1/2017</td>
<td>CheckMate-142 (NCT02060180)</td>
<td>Mismatch repair deficient and microsatellite instability high metabolic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan in patients ≥ 12 years of age</td>
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<tr>
<td></td>
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<td>9/2/2017</td>
<td>CheckMate-040 (NCT01658878)</td>
<td>HCC that has been previously treated with sorafenib</td>
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<tr>
<td></td>
<td></td>
<td>12/20/2017</td>
<td>CheckMate-238 (NCT01388908)</td>
<td>Adjunctive treatment for patients with melanoma with involvement of LN or patients with metastatic disease who have undergone complete resection</td>
</tr>
<tr>
<td>Ipilimumab + nivolumab</td>
<td>CTLA-4 + PD-1</td>
<td>9/30/2015</td>
<td>CheckMate-069 (NCT01927419)</td>
<td>BRAF V600 wild-type, unresectable or metastatic melanoma</td>
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<td>1/23/2016</td>
<td>CheckMate-067 (NCT03445025)</td>
<td>Unresectable or metastatic melanoma, regardless of BRAF V600 mutation status</td>
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<td>4/16/2016</td>
<td>CheckMate-214 (NCT02231749)</td>
<td>Intermediate- or poor-risk, previously untreated advanced RCC</td>
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<td></td>
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<td>12/18/2015</td>
<td>KEYNOTE-006 (NCT01846319), KEYNOTE-002 (NCT01704287)</td>
<td>Expanded approval as first-line therapy for unresectable or metastatic melanoma</td>
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<td>8/5/2016</td>
<td>KEYNOTE-012 (NCT01448334)</td>
<td>Recurrent or metastatic NSCLC that has progressed on/after platinum-containing chemotherapy</td>
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<td>10/24/2016</td>
<td>KEYNOTE-010 (NCT01905637), KEYNOTE-004 (NCT02142738)</td>
<td>1st-line therapy for metastatic NSCLC in which tumors have high PD-L1 expression (TPS ≥ 50%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and no prior systemic chemotherapy treatment for metastatic NSCLC, expanded 2nd-line treatment for metastatic NSCLC tumors with any level of PD-L1 (TPS ≥ 1%) as determined by an FDA-approved test, with disease progression on/after platinum-containing chemotherapy (patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for those aberrations)</td>
</tr>
<tr>
<td>Pembrolizumab (Keytruda®)</td>
<td>PD-1</td>
<td>3/15/2017</td>
<td>KEYNOTE-087 (NCT02453594)</td>
<td>Adult/pediatric refractory classical Hodgkin lymphoma or adult/pediatric classical Hodgkin lymphoma that has relapsed after 3 or more lines of therapy</td>
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<tr>
<td></td>
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<td>5/10/17</td>
<td>KEYNOTE-021 (NCT02039677)</td>
<td>In combination with pembexetin and carboplatin for previously untreated metastatic non-squamous NSCLC</td>
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<tr>
<td></td>
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<td>5/18/2017</td>
<td>KEYNOTE-045 (NCT02256436)</td>
<td>Locally advanced or metastatic urothelial carcinoma that has progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy; locally advanced or metastatic urothelial carcinoma in patients who are not eligible for platinum-containing chemotherapy</td>
</tr>
<tr>
<td>Drug name</td>
<td>Target</td>
<td>Date approved</td>
<td>Trial(s) based on</td>
<td>Indications</td>
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<td>----------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>Atezolizumab (Tecentriq*)</td>
<td>PD-L1</td>
<td>5/18/2016</td>
<td>IMvigor210 (NCT02108652)</td>
<td>Locally advanced or metastatic urothelial carcinoma that has progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy</td>
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<td></td>
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<td>10/18/2016</td>
<td>POPLAR (NCT01903993), OAK (NCT020008227)</td>
<td>Metastatic NSCLC that has progressed during or following platinum-containing chemotherapy; patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations</td>
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<tr>
<td></td>
<td></td>
<td>4/17/2017</td>
<td>IMvigor210 (NCT02108652)</td>
<td>1st-line treatment for locally advanced or metastatic urothelial carcinoma in cisplatin-ineligible patients</td>
</tr>
<tr>
<td>Avelumab (Bavencio*)</td>
<td>PD-L1</td>
<td>3/23/17</td>
<td>JAVELIN Merkel 200 (NCT02155647)</td>
<td>Metastatic Merkel cell carcinoma in patients ≥ 12 years of age</td>
</tr>
<tr>
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<td>5/9/17</td>
<td>JAVELIN Solid Tumor (NCT01772004)</td>
<td>Locally advanced or metastatic urothelial carcinoma that has progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy</td>
</tr>
<tr>
<td>Durvalumab (Imfinzi*)</td>
<td>PD-L1</td>
<td>5/1/2017</td>
<td>Study 1108 (NCT01693562)</td>
<td>Locally advanced or metastatic urothelial carcinoma that has progressed during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy</td>
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<tr>
<td></td>
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<td>2/16/2018</td>
<td>PACIFIC (NCT02125461)</td>
<td>Unresectable stage III NSCLC that has not progressed following concurrent platinum-based chemotherapy and radiation therapy</td>
</tr>
</tbody>
</table>

Abbreviations used: LN = lymph node, NSCLC = non-small-cell lung carcinoma, RCC = renal cell carcinoma, SCCHN = squamous cell carcinoma of the head and neck, HCC = hepatocellular carcinoma, dMMR = mismatch repair deficient, MSI-H = microsatellite instability-high.
Take home points.

• Immune checkpoint therapy is becoming very widespread.
• Will see its adverse affects more frequently, particularly HLH and other autoimmune phenomena

Autoimmune Lymphoproliferative Syndrome
Misdiagnosed as Hemophagocytic Lymphohistiocytosis
Thank you!
Haematology
Princess Alexandra Hospital (Hospitals)
Ipswich Road

WOOLLOONGABBA 4102
Phone: 0732402111
Fax:

Dear Doctor,

Dr Manoj - As discussed

Re: Mr F
Phone (Home): 07 - 3711 4080
Mobile:

Thank you for seeing him. He is 85 yrs, with persistantly low Hb and high BR.
He was in atr qe2 in early OCT with Hb 62--his BR at that stage was 56 and he was
jaundiced.
He had a t/f--7 no. of units--his Hb went up to 100 and then bugger me his Hb was snuck
back down to 93 only 3 wks later. He is jaundiced today too.
Oddly, he has B thalasemia despite having Asian DNA.
He gets soboe at running 100m and feels lethargic all th etime.
He has an appt at PAH haematol on 8-1-07 but I wonder if you could have a look at him
earlier.

Past Medical History
B thalasemia minor
colitis--on CT 10-07

If you have any queries regarding this referral, please feel free to contact me on Telephone