Table of Contents

Undifferentiated panel 1
CK7/20 table 2
Breast carcinoma 2
Lung adenocarcinoma 3
Mesothelioma 4
GYN 5
GI 6
GU and germ cell 6
Misc carcinomas (liver, kidney, adrenal) 7
Squamous and sarcomatoid carcinoma 8
Sustentacular cells 8
Derm 9
Soft tissue keratin+ 9
Soft tissue CD34+ 10
Soft tissue other markers 11
Soft tissue no good markers 12

Undifferentiated panel: Ca vs Mel vs La
Keratin AE1/3 mix, 90%+ of Ca
   Not CK7 or 20 or 5/6 to start with
   EMA, CEA as backups
S100
   95%+ of Mel, but 10% of Ca are +
   SOX10 may be better, more sensitive and specific
   HMB45, MelanA less sensitive, very specific
LCA or CD20 90% of lymphomas

Things that might be negative
Anaplastic large cell lymphoma - use CD30, ALK, CD3
Plasmacytoma – use CD138, kappa, lambda
Sarcomas – use various markers, esp vascular CD31, CD34
Spindled/sarcomatoid carcinoma – use CK5/6 and p63
Liver – use HepPar1
Adrenal – use Inhibin, MelanA, SF1
Seminoma/germinoma – use OCT3/4 or SALL4
**Carcinoma – primary site**
What is the DDx? Choose complementary antibodies (check the history first)

**CK7/20: USE THE TABLES**
Most use is for ADENOCARCINOMAS, Little data for undifferentiated Ca

### UNKNOWN PRIMARY: immunohistochemistry

<table>
<thead>
<tr>
<th>CK7+20+</th>
<th>CK7-20+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovary mucinous</td>
<td>90%</td>
</tr>
<tr>
<td>Transitional cell</td>
<td>65%</td>
</tr>
<tr>
<td>Pancreas adeno</td>
<td>65%</td>
</tr>
<tr>
<td>Cholangio</td>
<td>65%</td>
</tr>
<tr>
<td>Gastric adeno</td>
<td>40%</td>
</tr>
<tr>
<td>excluded tumors</td>
<td>≤ 5%</td>
</tr>
<tr>
<td>CK7+20-</td>
<td>CK7-20-</td>
</tr>
<tr>
<td>Ovary non-mucinous</td>
<td>100%</td>
</tr>
<tr>
<td>Thyroid (all 3 types)</td>
<td>100%</td>
</tr>
<tr>
<td>Breast</td>
<td>90%</td>
</tr>
<tr>
<td>Lung adeno</td>
<td>90%</td>
</tr>
<tr>
<td>Uterus endometrioid</td>
<td>85%</td>
</tr>
<tr>
<td>Embryonal</td>
<td>80%</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>65%</td>
</tr>
<tr>
<td>Transitional cell</td>
<td>35%</td>
</tr>
<tr>
<td>Pancreas adeno</td>
<td>30%</td>
</tr>
<tr>
<td>Cholangio</td>
<td>30%</td>
</tr>
<tr>
<td>excluded tumors</td>
<td>≤ 5%</td>
</tr>
<tr>
<td>Colorectal adeno; Ovary mucinous, Seminoma, Yolk sac tumor</td>
<td></td>
</tr>
</tbody>
</table>

### Breast Carcinoma

GATA3 90%, BRST2 (GCDFP15) 60%+, quite specific (salivary and skin adnexal tumors pos)
ER 75%+, PR 60%+ (lung most neg to focal/weak but up to 5% strong pos in one report)
S100 15%+, (lung neg)
CK7+20- 90% (lung is also 7+20-)
Mammaglobulin breast 85%, cholangio, GI, lung adenocarcina 10-20%

**ER, PR +**

Breast
Ovary
Endometrium
Papillary thyroid
Skin adnexal tumors
Sarcomas
Meningioma (PR only)
Solid-pseudopapillary neoplasm of pancreas (PR only)
**Breast carcinoma type**

E cadherin
- Ductal positive, Lobular negative
- Works for invasive and in situ

**Breast vs Lung Panel**
- BRST2 (60%) or GATA3 (90%) Breast pos Lung neg
- ER, PR favor breast but not sensitive
- TTF1 (70%) or Napsin (80%) - Lung pos Breast neg

**Metaplastic/Sarcomatoid Carcinoma**
- CK5/6 about 50%
- P63 60%
- AE1/3 40%
- Smooth muscle actin 70%

**Breast invasive vs in situ**
- Myoepithelial cells absent in invasion
- Smooth muscle actin stains myoepithelial cells; myofibroblasts frequently confusing
- Calponin cytoplasmic, a bit more specific than actin, easier to interpret at low power than p63
- P63 nuclear, most specific but may be harder to see at low power if not strong
- Calponin vs p63: personal preference or use both
- Occasionally get divergent results
  - Usually go with the positive

**Breast papilloma vs in situ**
- Calponin and/or p63
  - Are myoepithelial cells present throughout the lesion?

**Lung Adenocarcinoma**
- CK7+20- 90%, TTF1 70% (also thyroid +), Napsin 80% (also some RCCa +)
- CD56 5%, CK5/6 10%, p63 0-25% focal, PAX8 neg

**Lung squamous Ca, both basaloid and usual types**
- CK7-20- 70% (CK7+20- 25%)
- TTF1/Napsin neg, CD56 0-10%, PAX8 neg
- P63, 34BE12 and CK5/6+ 100%

**Lung small cell (oat cell) Ca**
- CK7-20- 90%, CK20 rare
- TTF1 90%, CD56 95%
- P63 neg, CK5/6 neg, 34BE12 scattered pos cells 12%, no confluent positive cases
- Synaptophysin 50%, Chromogranin 40%
- Keratin usually absent to patchy or dot like

**Oat vs Merkel cell**
- TTF1 Oat 90%, Merkel neg
- CK20 Oat neg, Merkel 90%
- Keratin may be dot like for both
- Chromogranin and synaptophysin variable in both
- Merkel 35-75% pos for TdT, do not confuse with ALL
**Mesothelioma**

Reactive vs neoplastic mesothelium:
- EMA, IMP3, Glut1, p53: favor mesothelioma if positive
- Desmin favors reactive if positive

<table>
<thead>
<tr>
<th>Markers</th>
<th>Pleural Mesothelioma</th>
<th>Lung Adenoca</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calretinin</td>
<td>90% (nuclear)</td>
<td>15%</td>
</tr>
<tr>
<td>CK5/6</td>
<td>90% (Benign mesos freq neg)</td>
<td>10%</td>
</tr>
<tr>
<td>D2-40 (podoplanin)</td>
<td>90%</td>
<td>0-7%</td>
</tr>
<tr>
<td>WT1</td>
<td>90%</td>
<td>25%</td>
</tr>
<tr>
<td>TTF1 (nucl) / Napsin (cytopl)</td>
<td>neg</td>
<td>70-80%</td>
</tr>
<tr>
<td>CD15</td>
<td>very rare</td>
<td>95%</td>
</tr>
<tr>
<td>CEA</td>
<td>very rare</td>
<td>90%</td>
</tr>
<tr>
<td>BerEp4</td>
<td>15%</td>
<td>95%</td>
</tr>
<tr>
<td>MOC31</td>
<td>10%</td>
<td>100%</td>
</tr>
<tr>
<td>B72.3 (TAG72)</td>
<td>5-15%</td>
<td>85%</td>
</tr>
</tbody>
</table>

**Lung vs Mesothelioma Panel**

Two or three of each of meso pos and lung pos markers should be enough

WT1 not useful vs lung

**D2-40**

- Kaposi sarcoma 100%
- Angiosarcoma 72%
- Seminoma 100%
  - Nonseminomatous germ cell negative
- Mesothelioma 90%
  - Lung adenocarcinoma 0-7%
  - Various carcinomas 20-40%
- Dermatofibroma 100%

<table>
<thead>
<tr>
<th>Markers</th>
<th>Ovary serous</th>
<th>Peritoneal mesothelioma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calretinin</td>
<td>7-34%, rare in our studies</td>
<td>100% (nuclear)</td>
</tr>
<tr>
<td>CK5/6</td>
<td>17%</td>
<td>100%</td>
</tr>
<tr>
<td>Thrombomodulin</td>
<td>30%</td>
<td>74%</td>
</tr>
<tr>
<td>PAX8</td>
<td>75-90%</td>
<td>9% (weak)</td>
</tr>
<tr>
<td>BerEp4</td>
<td>100%</td>
<td>9%</td>
</tr>
<tr>
<td>CD15</td>
<td>60%</td>
<td>neg</td>
</tr>
<tr>
<td>S100</td>
<td>27%</td>
<td>neg</td>
</tr>
<tr>
<td>B72.3 (TAG72)</td>
<td>80%</td>
<td>neg</td>
</tr>
<tr>
<td>MOC31</td>
<td>97%</td>
<td>3%</td>
</tr>
</tbody>
</table>

WT1 stains both (but good for ovary vs breast)

**Ovary serous vs mesothelioma panel**

BerEp4 Ovary+
MOC31 Ovary+
PAX8 Ovary+
Calretinin Mesothelioma+
GYN
Ovary vs Breast PAX8
Ovary surface epithelial carcinomas 70-100%
  Only mucinous 10-59%
Breast negative
Ovary Serous Ca
CK7+20- 100%
WT1 90%
  90% mesotheliomas, 25% lung adenoca, 5% breast
  Neg: colorectal, endometrial (incl pap serous), panc, bile duct, ovary mucinous

WT1 other reactivity
90% DSRCT
75% Wilms
55% Rhabdo
12% Neuroblastoma
0% PNFT
30% Burkitt and lymphoblastic
Pos AML
Angiosarcoma (cytoplasmic)

Ovary Mucinous
CK7+20+ 95%
MUC2 and MUC5AC various mucinous tumors +
  Ovary, appendix, colon, breast, stomach, endocervix
CDX2 mucinous ovary and GI tract all sites, pancreas +

Ovary CK7/20
Serous 7+20- 100%
Mucinous 7+20+ 95% (rule out stomach, pancreas, bile duct)
Colorectum 7-20+ 90%

Endometrial vs Endocervical (applies to glandular areas only)

<table>
<thead>
<tr>
<th></th>
<th>Endometrial</th>
<th>Endocervical</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER and vimentin</td>
<td>Usually diffuse pos</td>
<td>Usually neg or focal</td>
</tr>
<tr>
<td>P16 and CEA</td>
<td>Usually neg or focal</td>
<td>usually positive</td>
</tr>
</tbody>
</table>

Endometrial stromal vs Smooth muscle

<table>
<thead>
<tr>
<th></th>
<th>Muscle</th>
<th>Stromal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caldesmon</td>
<td>70%</td>
<td>5%</td>
</tr>
<tr>
<td>CD10</td>
<td>35%</td>
<td>95%</td>
</tr>
<tr>
<td>Desmin</td>
<td>90%</td>
<td>only in areas of muscle differentiation</td>
</tr>
<tr>
<td>B-catenin</td>
<td>neg</td>
<td>50-100%</td>
</tr>
</tbody>
</table>

Complete mole p57 neg vs partial mole and hydropic change p57 pos
MUC4 may be useful for identifying implantation site trophoblast
**GI Tract**

**Colorectum**
CK7-20+ 90%
MUC2 and MUC5AC various mucinous tumors +
   - Ovary, appendix, colon, breast, stomach, endocervix

**CDX2**
Colorectal >90%
Mucinous carcinomas of all organs including ovary, pancreas positive from 40-100%
<5% lung, prostate, breast, ovarian serous
Carcinoids: ileum and appendix >90%, other sites variable but frequently negative, lung negative
   - TTF1 stains 50% of pulmonary and 0% of GI.

**Stomach, Pancreas, Bile Duct**
No great markers
Wide range of CK7&20
Stomach 50%+ HepPar1
CA19-9 not specific for pancreas
   - Pos: Colon, ovary, lung, cholangio
   - 0-5%: Liver, breast, mesothelioma
Esophageal adenocarcinoma frequently TTF1 and napsin +

**GU & Germ Cell**

**Prostate – well/mod diff**
PSA or NNX3.1 and PSAP (prost acid phos) 95% pos
All very specific, one is usually enough if untreated, mod diff carcinoma
ERG very specific but 50% sensitive

**Prostate vs TCCa (high grade or treated Ca)**
For poorly diff TCCa: GATA3 may be most sensitive and specific
   - Backups p63 (85%) and HMWCK (CK5/6 or 34BE12 60%)
   - Uroplakin and thrombomodulin do not work for poorly diff TCCa
For poorly diff prostate ca, NNX3.1 more sensitive (>90%) than PSA (may be neg in 10%)
   - Both very specific

**Prostate Ca vs benign**
In general, for small foci, IPOX can prove benignancy but not prove malignancy
   - Small foci that stain as cancer are usually best left at ASAP (see surgpathcriteria)
Basal epithelial cells (not myoepithelial cells) absent in carcinoma
   - High molecular weight keratin - 34BE12 or CK5/6 cytoplasmic, p63 nuclear
   - Basal cells may be patchy
   - Presence of a basal layer virtually rules out invasive Ca (Gold standard?)
   - Intraductal carcinoma is an exception (see surgpathcriteria)
   - Rare cases of prostate carcinoma reported as p63 positive
      - Not a basal layer, but single layer glands
      - HMWCK negative, Racemase positive

**P504S (Racemase, AMACR)**
   - Positive in Ca and PIN, negative in benign
   - At least moderate, circumlumenal stain
   - Faint or patchy stain may be seen in benign
   - Lots of other carcinomas stain – this is not specific for prostate origin

**PIN2-PIN4 cocktails**
   - P504S (cytoplasmic), p63 (nuclear) +/- high molecular weight keratin
   - Especially useful if only one slide
   - P504S helps highlight the area of interest – go down and look for basal cells
   - For small foci, destain H&E instead of recutting block
Germ cell tumors

General
- EMA neg
- SALL4, OCT3/4 and CD30 are quite specific for germ cell
- PLAP and ckit stain many other carcinomas also

Seminoma - Keratin dots, focal or negative, rarely strong and diffuse
Embryonal Ca - HCG, AFP 20-30%, serum test may be better
Yolk sac Ca - AFP may be scant, serum test may be better

Germ cell tumors differential, % positive

<table>
<thead>
<tr>
<th></th>
<th>Sem.</th>
<th>EmbCa</th>
<th>YST</th>
<th>ChorioCa</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD117, ckit</td>
<td>90</td>
<td>0</td>
<td>0</td>
<td>0 few cases</td>
</tr>
<tr>
<td>D2-40, podoplanin</td>
<td>100 diffuse</td>
<td>30 focal</td>
<td>0</td>
<td>0 few cases</td>
</tr>
<tr>
<td>OCT3/4, POU5F1</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SALL4</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100 few cases</td>
</tr>
<tr>
<td>NANOG</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SOX2</td>
<td>0</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CD30</td>
<td>5</td>
<td>90</td>
<td>20</td>
<td>0 + few cases</td>
</tr>
<tr>
<td>CK7</td>
<td>5</td>
<td>80</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Glypican 3</td>
<td>0</td>
<td>0-8</td>
<td>100</td>
<td>30-100</td>
</tr>
<tr>
<td>EMA</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>50</td>
</tr>
</tbody>
</table>

Miscellaneous

Renal cell carcinoma
- CK7-20- 80% neg for both
- Keratin, EMA, CD10 90% but not specific
- PAX8 >80% (best for mets)
- SF1, CDX2, P63 negative
- RCCma 85%? (not in our hands)

Major types of RCCa (see surgpathcriteria for details and other types)

<table>
<thead>
<tr>
<th></th>
<th>Vimentin</th>
<th>CD117</th>
<th>CK7</th>
<th>CAIX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear cell</td>
<td>&gt;85%</td>
<td>&lt;5%</td>
<td>neg/focal</td>
<td>100%</td>
</tr>
<tr>
<td>Papillary</td>
<td>&gt;90</td>
<td>&lt;20</td>
<td>20-80</td>
<td>50%</td>
</tr>
<tr>
<td>Chromophobe</td>
<td>0</td>
<td>&gt;80%</td>
<td>&gt;70</td>
<td>neg</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>0</td>
<td>&gt;90%</td>
<td>neg/scat</td>
<td>neg</td>
</tr>
</tbody>
</table>

Hepatocellular Ca
- 70-90% HepPar1
  - 50% gastric
  - Occasional adrenal, yolk sac, colon, lung, ovary, endocervix
  - CholangioCa and pancreatic Ca can be + in up to 15%
- 85-100% Arginase1
  - CholangioCa and pancreatic Ca 0-8%
- <20% EMA, CD15, mCEA, MOC31
  - 80% mets and cholangiocarcinoma are positive for these markers
- <50% Canalicular staining: CD10 & pCEA, quite specific if branching
- 88% Glypican 3
  - Hepatic adenoma, FNH, cirrhosis negative
  - Other carcinomas 3%

CD34 stains sinusoidal lining in HCC but not normal sinusoid lining cells
**Keratin and EMA**

Keratin+ EMA-
- Hepatocellular Ca
- Germ cell tumors
- Granulosa cell tumor (keratin 30-50%)

Keratin- EMA+
- Meningioma
- Pulmonary sclerosing hemangioma (keratin+/–)
- Small cell ca and renal cell ca frequently EMA strong, keratin weak

**Adrenal cortical carcinoma**

SF1 85%, PAX8 negative
- MelanA, Inhibin 90% - less in carcinomas than adenomas?
- Calretinin, Synaptophysin 60-90%
- Keratin, EMA 0-15%

**CD10**

RCCa 90%
- Endometrioid ovary, prostate, HCCa, TCCa, SqCC 50-60%
- Melanoma, oat cell, pancreas 30-50%
- Lung adeno, colorectal, breast, serous ovary, stomach 10-20%
- Several sarcomas may stain (MFH, fibrosarcoma, MPNST…)

**Thyroid Ca**

Follicular or papillary - TTF1, thyroglobulin+
- Medullary - TTF1, calcitonin, chromogranin +

**Thymus**

Thymoma PAX8+, p63+, CD5 neg except B3 may be positive
- Thymic carcinoma PAX8+, p63+, CD5+
- Lymphocytes of normal thymus and thymoma have immature T phenotype

**Squamous Ca – all sites**

Can’t separate sites by IPOX
- P63, CK5/6 and 34BE12 more sensitive than AE1 or CAM5.2
- Majority are CK7-20-, PAX8-
- Cutaneous CEA-

**Spindled/sarcomatoid Ca**

CK5/6 and p63 frequently better than AE1
- About half are keratin negative
- About half may be smooth muscle actin positive

**Sustentacular cells (S100+, quite specific if definite)**

Paragangioma
- Esthesioneuroblastoma
- Neuroblastoma
- Carcinoid (infrequent)
- R/O interdigitating cells
**Derm IPOX - selected topics**

**DF vs DFSP**  
Factor 13a, increased in DF, not in DFSP  
Not easy to interpret  
Lesional cells or reactive cells? Entrapped around edges in some cases?  
CD34 - 75% DFSP  
Occasional cases seem to have a bit of both F13a and CD34  
D2-40 DF positive, DFSP negative/weak (one report)  
Nestin DFSP positive, DF neg/focal

**Desmoplastic melanoma**  
S100, SOX10 95-100%  
Both stain nerve sheath tumors  
Interdigitating cells S100+, SOX10 neg  
HMB45, MelanA neg or almost always neg  
Literature mixes desmoplastic with spindled  
Spindled melanomas usually pos for HMB45 and MelanA  
May have SMA+ myofibroblasts

**Intraepidermal melanocytic processes**  
MelanA, MITF and SOX10 are better than S100  
CK5/6 is a good complementary stain  
Use a red chromogen to avoid mistaking melanin pigment for positive stain  
Some reports of MelanA nonspecificity in actinic keratoses

**Dermal nevus vs invasive melanoma**  
Dermal nevus HMB45 neg, Ki67 <5%  
Melanoma frequently HMB45 pos, Ki67 >10%  
Ki67 may stain reactive lymphocytes etc

**Atypical fibroxanthoma**  
Defined as keratin, S100 negative  
Should also be p63, SOX10 neg  
Spindled, not desmoplastic, melanoma usually the differential  
Spindled carcinomas 50% keratin negative  
CD68 50% (Histiocyte marker, nonspecific – also in carcinoma, melanoma)  
CD163 better  
Smooth muscle actin 40%  
Leiomyosarcoma, some spindled SCC +  
CD10 and Procollagen 1 >90%, strong reactions appear relatively specific

**BerEp4** BCC and sebaceous carcinoma +, SCC neg

**Soft tissue tumors Keratin+**

**Synovial sarcoma**  
Keratin, EMA: Biphasic 100%, Monophasic 50%  
S100 30%  
TLE1 95%, occasionally in schwannoma, sft/hpc  
Temperamental IPOX stain, FISH is better  
CD99 50% (not specific, see CD99 and bcl2 notes below)  
bcl2 >90% (not specific, see CD99 and bcl2 notes below)
**Epithelioid sarcoma (both proximal and distal)**
Keratin, EMA essentially 100%, INI1 negative
CD34 50%, Carcinomas are negative

**(Intra-abdominal) desmoplastic small round cell tumor (DSRCT)**
Co-expresses desmin and keratin >90%
WT1 90%, CD15, BerEp4 70%
Calretinin, CK5/6 0-15%
CD99 35% (not specific, see CD99 and bcl2 notes below)

**Other keratin+ soft tissue tumors**
Inflammatory myofibroblastic tumor 30-77%
Extra-renal rhabdoid tumor 100% (INI1 loss in 85%)
Epithelioid angiosarcoma 0-50%
May also be seen in nerve sheath sarcomas (35%)
Occasionally seen in MFH (up to 17%) and smooth muscle tumors (dot-like)
Rhabdomyosarcoma reported 5-50%

**Soft tissue – CD34+**

**Vascular**
ERG new marker, may be most sensitive and specific
CD31 does well on high grade tumors
Also stains histiocytes
CD34 does better on lower grade tumors
Stains various other tumors
D2-40 lymphatic marker, stains 100% of Kaposi and 70% of angiosarcomas
Frequently use multiple markers
Epithelioid hemangioendothelioma – frequently only the lumens stain
Keratin 30-50% esp epithelioid tumors

**GIST**
DOG1 appears to be more sensitive and specific than CD117 or CD34
CD117 (c-kit) 90%
Quite specific among spindle cell tumors
Stains lots of carcinomas, melanomas
CD34 75%
Quite specific vs carcinoma, melanoma (better for epithelioid tumors)
Stains lots of spindle cell tumors

**Epithelioid sarcoma CD34 50% (see above under Soft Tissue Keratin+)**

**DFSP** CD34 75% (see above, Derm lesions)

**Solitary fibrous tumor / HPC**
CD34 SFT 90%, HPC 75%
STAT6 appears to be very sensitive and specific
CD99, bcl2 90% (not specific, see below)
Neg: keratin, actin, desmin, S100

**Spindle cell lipoma / Pleomorphic Lipoma**
CD34 100%
Other fatty tumors only scattered dendritic cells
Some dediff liposarcs positive
CD99, bcl2 >90% (not specific, see below)
Pleomorphic hyalinizing angiectatic tumor (PHAT)
CD34 80% large cells+
Factor 13a many pos small spindle cells
S100, keratin, actin neg

Mammary type myofibroblastoma
CD34 90%+
Desmin pos
Smooth muscle actin variable
Keratin, S100 negative

Soft tissue tumors - other markers +

Rhabdomyosarcoma
Desmin, muscle specific actin 50-100%
   Myogenin more specific, less sensitive
   SMA occasional + cells
CD56 50-100%
Keratin 5-50%
CD99 0-50%

Nerve sheath
S100, SOX10
   Benign virtually 100%, Malignant 30-50%
HMB45, MelanA pos indicates spindled melanoma
   (Pigmented nerve sheath tumors also positive)
   Negative result is indeterminate
CD34 stains some dendritic cells but not typically the neoplastic cells
   True S100+ CD34+ is unusual phenotype
Perineurioma: CD34+, EMA+(may be focal, faint), GLUT1+, S100 neg

PNET/Ewing
CD99 >90% (Not specific)
Keratin 15%
S100, synaptophysin 0-50%, chromogranin neg
Actin, desmin very rare
IN11: PNET/Ewing, Wilms, DSRCT 100%; Rhabdoid tumor 0%
FLI1 specific but not sensitive

CD99: soft tissue tumors
>90%: SFT, Sp cell lipoma, PNET/Ewing
20-60%: Synovial sar, HPC, MFH, Osteosar, Fibrosar, Leiomyosar, DSRCT
Before you use CD99, be sure it distinguishes between your candidates

bcl2: soft tissue tumors
>90%: Kaposi, Leiomyosar, Spindle cell lipoma, GIST, SFT, Synovial sar, Melanoma,
   Nerve sheath tumors, PNET
50%: DFSP, MFH, Fibrosar
Before you use bcl2, be sure it distinguishes between your candidates

Angiomyolipoma/PEComa (Perivascular Epithelioid Cell – oma)
HMB45, SMA definitional
MelanA, MITF pos
S100 variable
Atypical lipomatous tumor and dedifferentiated liposarcoma
MDM2 & CDK4 95-100% but difficult to interpret
   FISH is better for MDM2
Myxofibrosarcoma 40%, MFH 10%, Spindle cell lipoma 10%, Myxoid liposarcoma 4%
Pleomorphic liposarcoma neg
p16 reported as sensitive and more specific than MDM2 staining

Fibromatosis beta catenin 80-90% (nuclear), smooth muscle actin variable
   Most others in ddx negative except SFT and synovial sarcoma
   S100, CD34, CD117 neg

Desmoplastic small round cell tumor
Desmin and keratin pos, see above under Soft Tissue Keratin+

Alveolar soft part sarcoma
TFE3 strong nuclear +, muscle markers variably positive

Low grade fibromyxoid sarcoma & sclerosing epithelioid fibrosarcoma
MUC4 relatively sensitive and specific, except for 30% of monophasic synovial sarcoma

Soft tissue – No good markers

MFH - CD68 stains cells with lysosomes, not specific
   CD163 stains only 4%
Fibrosarcoma
IPOX mostly to rule out things in the differential dx of this group