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Pharmac:

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Re – Gastrointestinal cancer systemic therapy

The gastrointestinal special interest group met with representatives of Pharmac last year and undertook to communicate with Pharmac on a regular basis with regards to our assessment of the landscape of systemic anti-GI cancer therapy including horizon scanning.

2020 has been a unique year; please accept our apologies that it is November already.

Medical oncologists and nurse practitioners who treat gastrointestinal cancers continue to be frustrated by the increasing gap between what is available and funded for New Zealand patients with gastrointestinal cancers and what is available in similar jurisdictions – for example Australia's PBS or UK's NICE. We are barely keeping pace with the WHO's essential medicine list.

This disparity presents challenges to patients and their whanau as self-funding at "retail" is out of the reach of most except the wealthiest including, as it must, by Ministry of Health edict, the administration costs in a private day unit also. This serves to further exacerbate the inequity in outcomes between underserved populations and the privileged.

The subsequent moral injury experienced by involved clinicians cannot be underestimated. Knowing that patients are no longer receiving cancer care as per international guidelines and being powerless to effect change is increasingly common. Please do not accept our silence as compliance.

New Zealand is a world leader in our pandemic response and we have as a country demonstrated a willingness to spend generously to gain health benefits for the most vulnerable. If New Zealanders were asked, we feel they would feel similarly about cancer care and would not accept an inferior standard of care for expedience.

As a direct result of our pharmaceutical access deficit, we are no longer able to participate in global clinical research. New Zealand patients should be well placed to access clinical trials while our health system is operating 'as usual' without the devastation experienced by many countries mid-pandemic. However, our patients' pathways preclude inclusion due to no longer having access to standard best evidenced first line therapies in many diseases including metastatic colorectal cancer (cetuximab/bevacizumab), pancreatic ductal adenocarcinoma (nab-paclitaxel) and her-2 positive gastric cancer (trastuzumab).

Please find, to follow, identified gaps in drug availability including drugs declined, drugs for which a biosimilar should provide access, drugs awaiting funding with assigned priorities, drugs that await assessment and are funded elsewhere, and horizon scanning – things to watch for in the future.

Nab-paclitaxel is a standard first-line option in poorer performance status patients[i] and useful second-line therapy in post-FOLFIRINOX treated patients. An application for funding for nab-paclitaxel was submitted in November 2014, sadly, despite metastatic pancreatic ductal adenocarcinoma being recognised as a cancer in which New Zealand patients' survival is falling[ii] – in contrast to other similar countries – this application was declined. Nab-paclitaxel has had a PBS listing since November 2014 and has been available with NICE guidance since September 2017.

Bevacizumab is an important part of first line therapy for metastatic colorectal cancer providing increased survival[iii], prolonged disease control[iv] and increased downstaging[v] to provide for curative intent resection. Pre-treatment with bevacizumab, outside of all-ras/raf wild-type left-sided metastatic colorectal cancer, is a pre-requisite for most if not all second line metastatic colorectal cancer trials. Bevacizumab has had a PBS listing since 2009.

GISIG has submitted before regarding **trastuzumab** in her-2 over-expressing gastric cancer. Bio-similars are increasingly available with significant cost-saving. GISIG would ask that patients with metastatic Her-2 over-expressing gastro-oesophageal adenocarcinoma be considered with urgency. The ESMO magnitiude of clinical benefit scale considers doublet chemotherapy with trastuzumab in her-2 positive metastatic gastric cancers at the top end of its scale due to the achieved hazard ratio in an overall survival endpoint and sustained improvement in quality of life. Pragmatic interpretation of the TOGA trial has led to funding in comparable jurisdictions e.g. focus on the IHC 3+ sub-group by NICE. NICE and PBS have provided access to trastuzumab for some time now.

Currently raltitrexed and cetuximab are in 'no-man's' land.

Cetuximab has been batted around for some time. As evidence has evolved an increasingly small population with focussed survival benefit has been identified[vi]. This has resulted in the use of cetuximab being restricted to left-sided primary tumour location all ras/raf wild-type cancers in international guidelines. PTAC have declined application twice. CaTSoP have recommended funding with a medium priority. We are in a Kafkaesque situation where one of the reasons for delay or potential decline of funding for an anti-EGFR antibody in left-sided colon cancer is that PBS (listing since 2011) NICE (listing since 2017) have not taken into account primary tumour location. We await the "options compared" process completion.

Raltitrexed is a rarely used medicine; until recently, funded access was provided via NPPA for the infrequent patient felt to potentially benefit in the setting of reaction, or unacceptable risk of reaction, to fluoro-pyrimidines. Sadly, despite an average of less than one patient requiring access a year over many years, this was felt to no longer meet the criteria for NPPA. A clinician driven application was submitted as requested – low priority has been assigned – and we wait. Patients with metastatic colorectal cancer and cardiac comorbidities subsequently lack therapeutic options. Again, this disproportionately affects already disadvantaged populations.

GISIG would like to add support to the consumer driven application for access to an **anti-PD-1/anti-PD-L1 agent e.g. pembrolizumab** for treatment of those with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) cancers. There is increasing evidence that this is a useful strategy with prolonged disease control and subsequent survival when given in either first or later lines of therapy[vii] for both dMMR colorectal[viii] and non-colorectal[ix] cancers.

We await with interest NICE review (due for publication June 2021[x]) and PBS re-assessment in light of Keynote-177[xi].

Medical oncologists look to Australia; we are members of the same College (RACP) and the same research community (AGITG). However, Australian patients enjoy access to modern pharmaceuticals that New Zealand patient can only access with gold-plated insurance or large bank balances. Currently, New Zealand patients are missing out on atezolizumab/bevacizumab for patients with hepato-cellular carcinoma which will shortly have PBS listing.

Hepatocellular carcinoma remains a serious public health issue for New Zealand. Incidence is increasing due to both infectious hepatitis and non-alcoholic fatty liver disease. Hepatocellular carcinoma is a disease that disproportionately affects disadvantaged communities. Recent progress in systemic therapies in unresectable hepatocellular carcinoma have provided real hope. The IMbrave150 study[xii] compared the **atezolizumab-bevacizumab** combination therapy with **sorafenib** (the international - not funded in New Zealand – standard of care, available on PBS); overall survival, progression free survival, disease control rate and quality of life were all improved in the combination arm.

GISIG wishes to draw attention to "watch this space" coming data. More detail will be provided as evidence matures.

Horizon scanning considerations

- Adjuvant nivolumab post CROSS chemo-radiotherapy and surgery in oesophageal adenocarcinoma with residual disease at time of surgery (non-pCR) – improved disease-free survival. Overall survival data immature[xiii].
- Anti-her-2 antibodies with FLOT – peri-operative chemotherapy for stomach/oesophagus adenocarcinoma – dramatically increased pCR rates, DFS/OS data immature[xiv].
- Combination anti-her 2 therapy for metastatic colorectal cancer[xv]
- Tumour agnostic therapies for rare targetable mutations, for example, Entrectanib[xvi]/larotrectanib[xvii] for the <1% of GI cancer patients with tumours with an NTRK fusion.
- BEACON[xviii] strategy for metastatic B-RAF mutant colorectal cancer; doublet therapy with encorafenib and cetuximab doubled overall survival.

Thank you for allowing us the opportunity for communication. Please accept this letter as our voice as advocates for New Zealanders with gastrointestinal cancers.

Yours truly,

Dr Kate Clarke and the undersigned
On behalf of GISIG (Gastrointestinal cancers special interest group)

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