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Pharmacological class effects of anticancer drugs: opportunities for decreasing healthcare spending

Daniel A Goldstein,[1] Leonard B Saltz,[2,3] Gregory R Pond,[4] Ian F Tannock [5,6]

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[1]Medical Oncology, Rabin Medical Center Davidoff Cancer Center, Petah Tikva, Central, Israel
[2]Medical Oncology, Memorial Sloan Kettering Cancer Center, New York, New York, USA
[3]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, USA
[4]Biostatistics, McMaster University, Hamilton, Ontario, Canada
[5]Medical Oncology, Princess Margaret Hospital Cancer Centre, Toronto, Ontario, Canada
[6]University of Toronto, Toronto, Ontario, Canada

Correspondence to
Dr Ian F Tannock;
ian.tannock@uhn.ca

ABSTRACT

In the field of general medicine, class effects, or therapeutic interchangeability, have been declared for several families of drugs including statins, calcium channel blockers and ACE inhibitors. The existence of such class effects enables healthcare payers to negotiate for substantially lower drug prices, thereby reducing financial toxicity, both at an individual and societal levels. Until now, the existence of class effects in oncology has been considered rare. Here, we review evidence from clinical trials that supports the existence of class effects for several types of anticancer drugs. These class effects in oncology should be exploited to reduce healthcare costs.

WHAT THIS STUDY ADDS

⇒ Several classes of anticancer drugs contain members that provide similar outcomes in clinical trials, suggesting that they are interchangeable.
⇒ Acceptance of interchangeability among members of a class of anticancer drugs could allow for considerable savings in cost, and improved access to treatment.

HOW THIS STUDY MIGHT AFFECT RESEARCH PRACTICE OR POLICY

⇒ Substitution of drugs in a class would allow substantial cost savings

INTRODUCTION

The high cost of anticancer drugs is a challenge for patients and healthcare payers that leads to financial toxicity and reduced access to effective treatment. Different tools have been developed in attempts to manage this problem, including formal health technology assessments such as cost-effectiveness analyses and value frameworks such as the European Society of Medical Oncology Magnitude of Clinical Benefit Scale.[1 2] Opportunities to reduce cost and increase access to effective treatments exist through interventional pharmacoeconomics, using strategies such as lower doses or less frequent schedules of certain drugs.[3 4] A strategy that has been effective elsewhere in medicine but has been explored rarely in oncology, is recognition of pharmacological class effects and therapeutic interchangeability as a tool to promote price competition and allow for the substitution of less expensive drugs within a class.

When one purchases a car, there are models of different size and performance made by different manufacturers, allowing the customer to choose based partly on price. This competition ultimately drives down prices within a market. There are many examples where several anticancer drugs with the same mechanism of action have been approved, thus creating an opportunity for competition on price. We propose that similar economic decision-making should be applied in oncology and that it could have a substantial impact on drug spending. Such strategies have been used for supportive drugs such as antiemetics and bisphosphonates, but for anticancer agents they have largely been restricted to the development and use of generic and biosimilar drugs. In this article, we first explore class effects and how they have been applied for the treatment of diseases other than cancer. We then demonstrate similar potential for relief of financial toxicity in oncology and improved access to effective treatment.

DEFINING DRUG CLASSES

While recognising that there is no uniformly accepted definition, the Evidence-Based Medicine Working Group defined a drug class as a group of drugs that share a similar structure and mechanism of action,[5] and where there is clinical evidence to support interchangeability. McAlister *et al* organised clinical evidence into a hierarchy, where the highest evidence level required a direct comparison in a randomised control trial (RCT), and lower levels of evidence required cross-trial comparisons with a placebo.[5]

The Evidence-Based Medicine Working Group provides specific examples, one of

Table 1 A hierarchy of evidence to support membership of a class effect for anticancer drugs (adapted from McAlister *et al*[5])

Level 1	Head-to-head RCT comparing drugs within a chemical class, with a clinically important endpoint.
Level 2	Head-to-head RCT comparing drugs within a chemical class, with a validated surrogate endpoint. Comparison across RCTs of drugs within a chemical class that were each compared with a placebo or to a former standard. Endpoints may be clinically important or possible surrogates.
Level 3	Comparison of subgroup analyses across RCTs of drugs within a chemical class that were compared with placebo or to a former standard. The endpoints may be clinically important or possible surrogates.
Level 4	Comparison of non-randomised studies, such as observational studies, using clinically important endpoints.

Clinically important endpoints are overall survival or quality of life. Possible surrogate endpoints are progression-free survival for advanced disease, disease-free survival for adjuvant therapy or response rate.
RCT, randomised controlled trial.

which is calcium channel blockers.[5] Drugs in this class all contain dihydropyridine rings and block the voltage-dependent calcium channels in cell membranes: the resulting clinical impact is to lower blood pressure. When different drug options exist within a class, barring a specific policy from the healthcare payer, the clinician will usually choose a specific drug based on what he/she considers the most favourable efficacy to toxicity ratio. This opinion may or may not be based on robust data. Marketing campaigns by manufacturers may influence clinical decision-making, but healthcare payers and hospitals have often used this opportunity to negotiate lower prices within a class, with reimbursement for only the cheapest effective drug.

In 2002, all American hospital pharmacies were invited to participate in a survey and over 90% of those responding reported having policies of therapeutic interchange.[6] These policies allow for automatic switching within a drug class, where similar therapeutic benefits had been accepted by the institution and were prevalent in both private and teaching hospitals. Among a long list, drugs included in such policies were proton pump inhibitors, statins, cephalosporin antibiotics and ACE inhibitors. ACE inhibitors decrease cardiovascular mortality in patients with heart failure due to left ventricular systolic dysfunction. It seems reasonable that therapeutic interchange programmes should be acceptable for cancer, given that such programmes are used in heart failure, also a disease with potentially fatal consequences.

LEVELS OF EVIDENCE TO DEMONSTRATE SIMILAR THERAPEUTIC EFFECTS IN ONCOLOGY

We have adapted the guidelines of the Evidence-Based Medicine Working Group to generate a set of criteria that would be sufficient to identify anticancer drugs within a class appropriate for substitutions. Most anticancer drugs have not been compared with a placebo, but to prior drug(s) of a different class with lower efficacy or greater toxicity, and we have extended this hierarchy to include those comparisons (table 1). For anticancer drugs, the clinically relevant endpoints are overall survival (OS) and quality of life; possible surrogate endpoints such as progression-free survival (PFS) and response rate have poor correlation with these endpoints.[7 8] Chemical structures are known, and their similarity is used to establish membership within a class. Each member of the class will have been approved (possibly for different treatment regimens or tumour types), and animal studies and phase 1 trials will have been performed to establish safety and to describe toxic side effects. Efficacy of each class member will have been demonstrated in at least one therapeutic scenario, and the major question required for support of drug substitution is the required level of evidence in support of clinical interchangeability where a different member of the class has proven effective.

INTERCHANGEABILITY IN ONCOLOGY

There are at least two examples where clinical interchangeability of anticancer drugs has been widely accepted: non-steroidal aromatase inhibitors (AIs) for treatment of oestrogen receptor positive (ER+) breast cancer and gonadotropin-releasing hormone (GnRH) agonists for treatment of prostate cancer. The two non-steroidal AIs, anastrozole and letrozole, are triazole derivatives that differ in potency and in degree of aromatase inhibition.[9] It is widely accepted that either can be used in clinical trials or clinical practice (eg, in drug combinations) that require use of an AI. There are four GnRH agonists in common clinical use for testosterone suppression in men with prostate cancer (or for inducing temporary menopause in young women with breast cancer): buserelin, goserelin, leuprolide and triptorelin. Each is a nonapeptide or deca-peptide analogue of GnRH (a decapeptide), and each is available in long-acting forms (3-monthly depot injections are widely used) that reduce serum testosterone to low levels in men. Many clinical trials for men with prostate cancer require them to be on androgen deprivation therapy, and either orchiectomy or any of these drugs are acceptable. Level 2 evidence appears to have been sufficient to justify this interchangeability: members of the class were evaluated in different RCTs against alternative

Table 2 Types of cancer where at least two drugs within a class are approved, and where cross-trial results of RCTs with time-to-event endpoints can be compared

Drug group/trial name	No. patients exp/cont.	Deaths exp/cont	HR (95% CI) for OS
Non-metastatic castrate resistant prostate cancer vs placebo			
Enzalutamide (PROSPER)[12]	933/468	288/178	0.73 (0.61–0.89)
Apalutamide (SPARTAN)[13]	806/401	178/107	0.75 (0.59–0.96)
Darolutamide (ARAMIS)[14]	955/554	148/106	0.69 (0.53–0.88)
Metastatic hormone sensitive prostate cancer with ADT			
Enzalutamide vs non-steroidal AI (ENZAMET)[16]	563/562	102/143	0.67 (0.52–0.86)
Apalutamide vs placebo (TITAN)[15]	525/527	83/117	0.67 (0.51–0.89)
Darolutamide vs placebo (ARASENS)[17]	651/655	229/304	0.68 (0.57–0.80)
Metastatic ER+breast cancer with fulvestrant vs placebo			
Palbociclib (PALOMA-3)[21]	347/174	201/109	0.81 (0.64–1.03)
Ribociclib (MONALEESA-3)[22]	484/242	222/142	0.73 (0.59–0.90)
Abemaciclib (MONARCH-2)[23]	446/223	211/127	0.76 (0.61–0.95)
Metastatic ER+breast cancer first line with AI vs placebo			
Palbociclib (PALOMA-2)[25]	444/222	Total 405	0.96 (0.78–1.18)
Ribociclib (MONALEESA-2)[26]	334/334	181/219	0.76 (0.63–0.93)
Abemaciclib (MONARCH-3)[28]	328/165	Total 252	0.75 (0.58–0.97)
first line Metastatic RCC: IO+TKI vs sunitinib			
Avelumab+axitinib (JAVELIN)[38]	442/444	109/129	0.80 (0.62–1.03)
Pembrolizumab+axitinib (KEYNOTE-426)[39]	432/429	193/225	0.73 (0.60–0.88)
Nivolumab+cabozantinib (CHECKMATE-9ER)[40]	323/328	121/150	0.70 (0.55–0.90)
Pembrolizumab+lenvatinib (CLEAR)[41]	355/357	74/106	0.66 (0.49–0.88)
second-line metastatic NSCLC: IO vs docetaxel			
Pembrolizumab; PD-L1>1% (KEYNOTE-010)[49]	690/343	584/309	0.70 (0.61–0.80)
Nivolumab; squamous without PDL1 selection (CHECKMATE 017)[50]	135/137	110/128	0.62 (0.47–0.80)
Nivolumab; non-Squamous without PDL1 selection (CHECKMATE 057)[50]	292/290	228/247	0.75 (0.63–0.91)
Atezolizumab; without PDL1 selection (POPLAR)[51]	144/143	121/120	0.76 (0.58–1.00)
Atezolizumab; without PDL1 selection (OAK)[51 52]	613/612	486/496	0.78 (0.68–0.89)
first line Metastatic NSCLC: IO vs CT			
Pembrolizumab; PD-L1>50% (KEYNOTE-024)[53]	154/151	103/123	0.62 (0.48–0.81)
Pembrolizumab; PD-L1>50% (KEYNOTE-042)[54]	299/300	Total 356	0.69 (0.56–0.85)
Cemiplimab; PD-L1>50% (EMPOWER)[55]	283/280	Total 175	0.57 (0.42–0.77)
Atezolizumab; PD-L1 High (IMpower-110)[56]	107/98	Total 101	0.59 (0.40–0.89)
Durvalumab; PD-L1>25% (MYSTIC)[57]	163/162	108/128	0.76 (0.56–1.02)
first line metastatic NSCLC (without PDL1 biomarker): IO+CT vs CT			
Pembrolizumab; non-squamous (KEYNOTE-189)[58]	410/206	Total 235	0.49 (0.38–0.64)
Pembrolizumab; squamous (KEYNOTE-407)[59]	278/281	225/248	0.71 (0.59–0.85)
Cemiplimab; all histologies (EMPOWER-lung)[60]	312/154	132/82	0.71 (0.53–0.93)
Atezolizumab; non-squamous (IMpower-130)[61]	451/228	226/131	0.79 (0.64–0.98)
Atezolizumab; squamous (IMpower-131)[62]	343/340	228/245	O.88 (0.73–1.05)
Atezolizumab; non-squamous; all pemetrexed (IMpower-132)[63]	292/286	137/154	0.86 (0.71–1.06)

Continued

Table 2 Continued

Drug group/trial name	No. patients exp/cont.	Deaths exp/cont	HR (95% CI) for OS
Atezolizumab; non-squamous: all bevacizumab (IMPower-150)[64]	359/337	179/197	0.78 (0.64–0.96)
First-line extensive stage SCLC (without PDL1 biomarker): IO+CT vs CT			
Atezolizumab (IMpower-133)[65]	201/202	138/158	0.76 (0.60–0.95)
Durvalumab (CASPIAN)[66]	268/269	210/231	0.75 (0.62–0.91)
Pembrolizumab (KEYNOTE-604)[67]	228/225	169/188	0.80 (0.64–0.98)
Metastatic melanoma: PD1 blockade vs CTLA4 blockade			
Pembrolizumab vs Ipilimumab (KEYNOTE-006)[68]	556/278	324/172	0.73 (0.61–0.88)
Nivolumab vs Ipilimumab (CHECKMATE-067)[69]	316/315	164/218	0.63 (0.52–0.76)
Metastatic head and neck cancer: IO vs CT			
Pembrolizumab (second-line: KEYNOTE-40)[70]	247/248	181/207	0.80 (0.65–0.98)
Nivolumab (second-line: CHECKMATE-141)[71]	240/121	133/85	0.70 (0.51–0.96)
second line metastatic squamous oesophageal cancer: IO vs CT			
Pembrolizumab (KEYNOTE-181)[72]	198/203	total 348	0.78 (0.63–0.96)
Nivolumab (ATTRACTION-3)[73]	210/209	160/173	0.77 (0.62–0.96)
First line metastatic squamous (no PDL1) oesophageal Ca: IO+CT vs CT			
Pembrolizumab (KEYNOTE-590)[74]	373/376	571	0.72 (0.60–0.88)
Nivolumab (CHECKMATE-648)[75]	321/324	135/204	0.74 (0.58–0.96)
second line metastatic urothelial cancer: IO vs CT			
Pembrolizumab (KEYNOTE-045)[76]	270/272	Total 334	0.73 (0.53–0.91)
Atezolizumab (IMvigor-211)[77]	467/464	324/350	0.87 (0.63–1.21)
First-line metastatic urothelial cancer: IO+CT vs CT			
Pembrolizumab (KEYNOTE-361)[78]	351/352	245/263	0.86 (0.72–1.02)
Atezolizumab (IMpower-130)[79]	451/400	235/228	0.83 (0.69–1.00)

ADT, androgen deprivation therapy; AI, aromatase inhibitor; CT, chemotherapy; IO, immunotherapy; NSCLC, non-small cell lung cancer; OS, overall survival; RCC, renal cell carcinoma; SCLC, small cell lung cancer; TKI, tyrosine kinase inhibitor.

treatments such as tamoxifen (for AIs) or orchiectomy (for GnRH agonists). It is important to note that National Comprehensive Cancer Network guidelines also recognise the existence of class effects for AIs and GNRH agonists.[10]

PROPOSED CLASS EFFECTS IN ONCOLOGY

We propose below additional opportunities for drug substitution within different classes of anticancer therapies, we provide the clinical trial data related to the similarity of clinical effects of proposed members of different classes of anticancer drugs. These data are summarised in table 2 and figures 1–3 demonstrate forest plots of the HRs to support these classes. While it is difficult to perform cross-trial comparisons, we have tried to select trials, and groups within trials, which are similar in inclusion and exclusion criteria. The examples that we provide are not a definitive list, rather some examples of class effects for consideration in the field of solid tumour oncology.

Androgen receptor inhibitors

Enzalutamide, apalutamide and darolutamide are structurally similar second-generation antiandrogens that have provided similar levels of benefit to men with prostate cancer (table 2; figure 1A,B).[11] Each of them has been shown in RCTs to delay appearance of metastases and improve OS in men with non-metastatic castrate-resistant prostate cancer and a PSA doubling time less than 10 months when added to standard androgen-deprivation therapy (ADT).[12–14] They each improve survival when added to ADT for men with hormone-sensitive prostate cancer.[15–17] Effect sizes in these trials were similar, and the drugs are well tolerated by most men. There are differences in side effects with a low incidence of seizures and more fatigue in men taking enzalutamide, a rash in men taking apalutamide, and claims of less falls and fractures with darolutamide, which does not cross the blood–brain barrier.[11 18] However, these differences are small, and after excluding the rare patient with a history

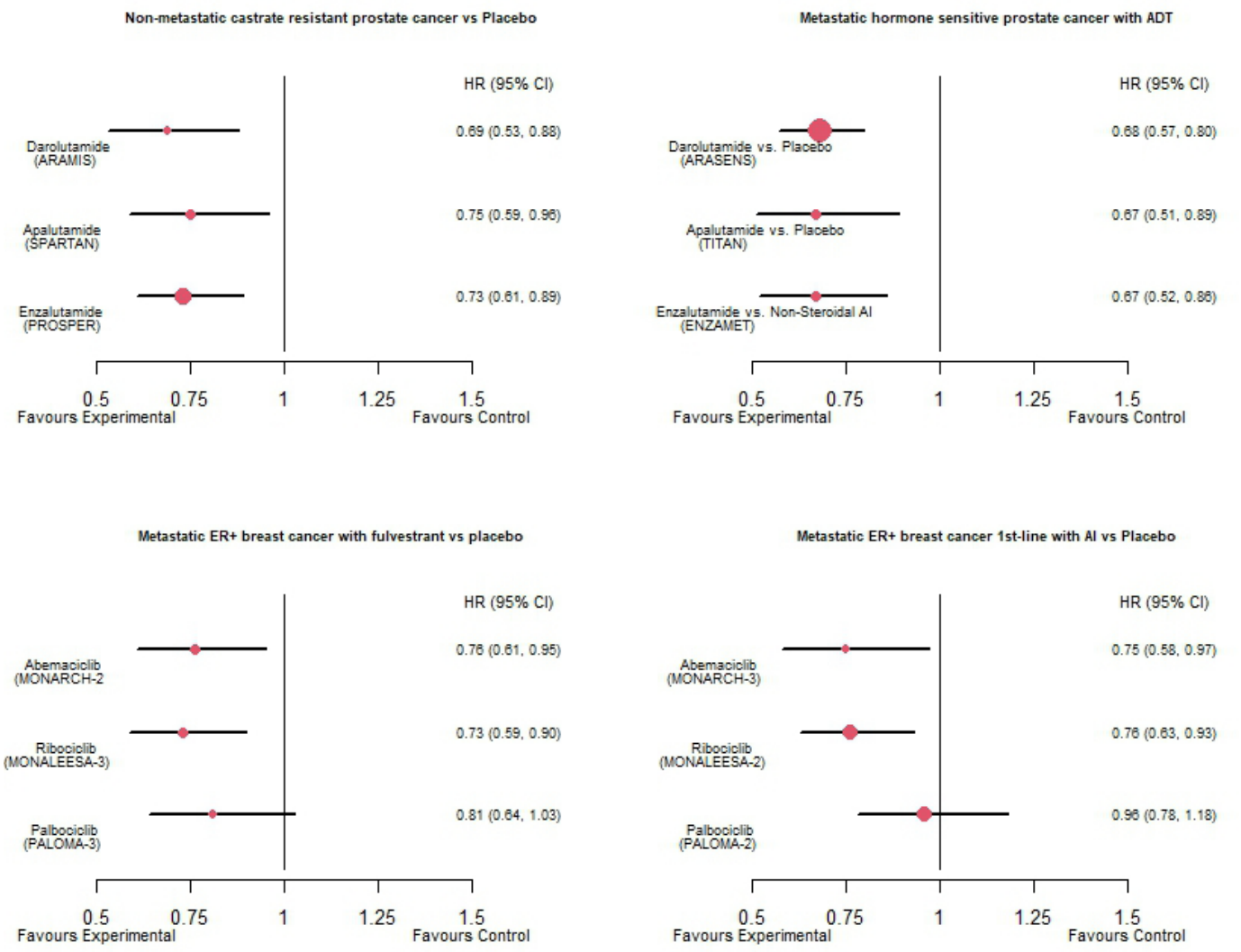

Figure 1 Forest plots of drug classes for androgen receptor blockers for prostate cancer and CDK4/6 inhibitors for breast cancer. The size of the point estimate is a weighted measure of the number of participants in the trial relative to the number of participants in the smallest trial in each group. ADT, androgen-deprivation therapy; CDK, cyclin-dependent kinase; ER+, oestrogen receptor positive.

of seizures, choice of treatment can be made on the basis of cost, favouring enzalutamide, which will be available in generic form in USA from 2026, and is already available as a generic in India and some other countries.

Cyclin-dependent kinase 4/6 inhibitors

Palbociclib, ribociclib and abemaciclib are structurally similar CDK4/6 inhibitors, with small differences in binding to their CDK4/6 target.[19] Marra and Curigliano have summarised similarities and differences in clinical effects of these agents observed in earlier clinical trials.[20] RCTs have shown that each drug leads to comparable improvements in OS (compared with placebo) for women with metastatic ER+ breast cancer when given with fulvestrant after disease progression on prior hormonal therapy (table 2; figure 1C).[20–23] Each drug has improved PFS compared with placebo when used with first-line hormonal therapy, with a significant effect (ribociclib), strong trend (abemaciclib) or minimal trend (palbociclib) to improve OS (figure 1D).[24–28] A factor that confounds cross-comparison of OS in these trials is treatment received by the control groups at time of disease progression. In the trials comparing first-line treatment of letrozole with palbociclib or ribociclib and placebo for advanced disease, only 27% and 34%, respectively, of controls received a subsequent CDK4/6 inhibitor.[24 26] Trials of adjuvant therapy have reported that abemaciclib and ribociclib but not palbociclib added to endocrine therapy leads to improvement in the primary endpoint of invasive disease-free survival.[29–32] Differences in outcome from a cross-comparison of clinical trials might be due to inherent differences in the efficacy of these drugs, to statistical variation about a similar level of effect, to variable bias arising from uneven dropout and informative censoring or to failure to provide optimal treatment at progression. Common side effects of these agents include fatigue, myelosuppression with consequent increase in

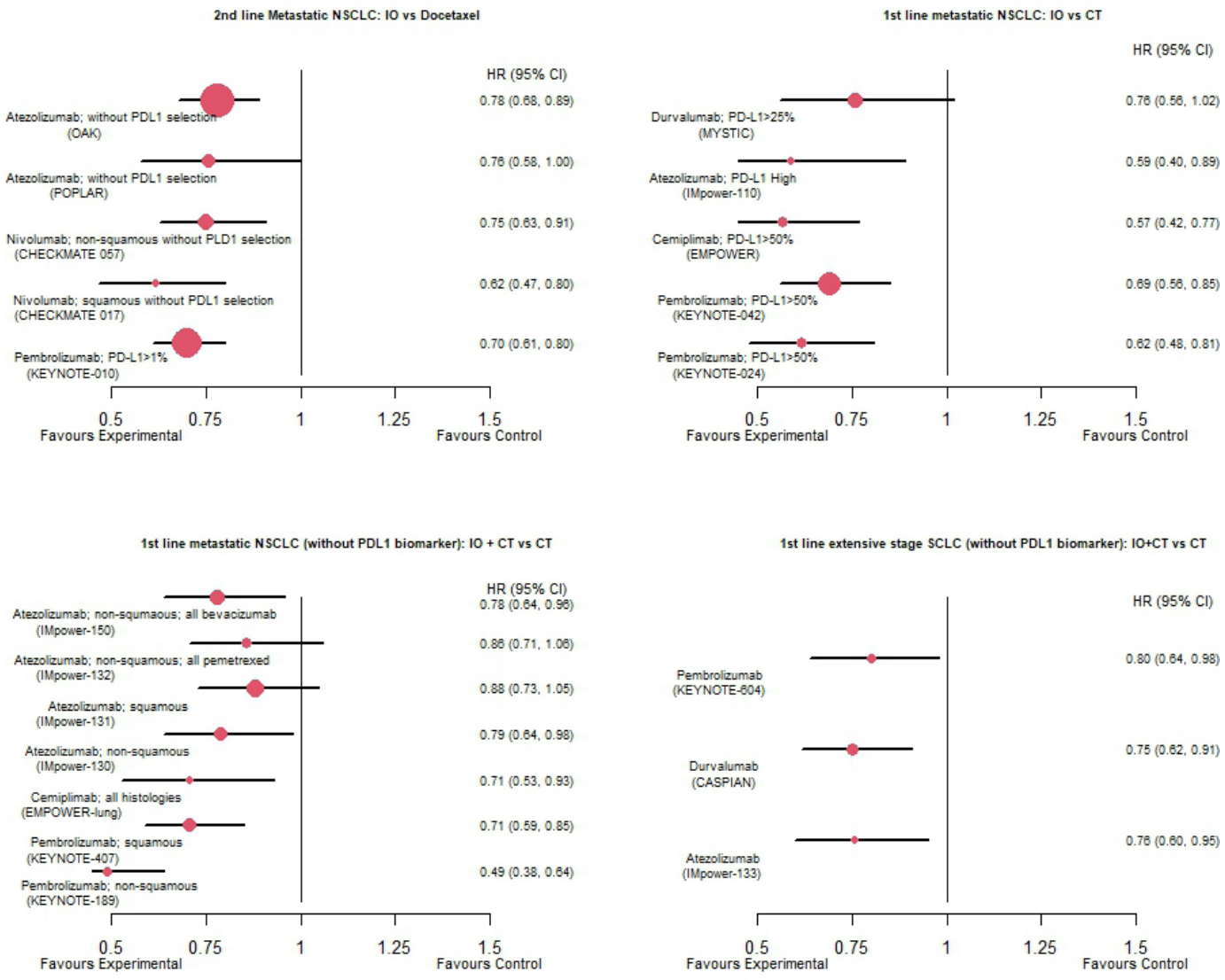

Figure 2 Forest plots of drug classes in lung cancer. CT, chemotherapy; IO, immunotherapy; NSCLC, non-small cell lung cancer.

infections (more common with palbociclib and ribociclib) and diarrhoea (more common with abemaciclib).[20 33 34] Ribociclib produces QT prolongation in 1%–3% of patients[20] and should be avoided in women at increased risk of cardiotoxicity. At present, drug substitution seems justified for most women when these agents are used with fulvestrant after prior lines of hormonal therapy for metastatic disease.

Epidermal growth factor receptor inhibitors

Erlotinib, gefitinib and osimertinib are small molecule selective inhibitors of *EGFR* used mainly in the treatment of epidermal growth factor receptor (*EGFR*)-mutated non-small cell lung cancer (NSCLC), while other drugs target multiple kinases including *EGFR*. There is evidence that outcomes using erlotinib or gefitinib are similar,[35] and they are generally accepted as being interchangeable. Osimertinib led to improved PFS and OS when compared with investigator's choice of erlotinib or gefitinib for treatment of *EGFR*-mutated NSCLC,[36] and should only be substituted by the older drugs if osimertinib is not available or affordable, as may occur in low-income and middle-income countries. Cetuximab and panitumumab are monoclonal antibodies that target *EGFR* used mainly for treatment of colorectal cancer. A head-to-head comparison of these agents in an RCT for chemotherapy-refractory *KRAS* wild-type colorectal cancer showed similar OS,[37] providing level 1 evidence of a class effect in this disease.

Immunotherapy and tyrosine kinase inhibitors combinations in kidney cancer

Four trials have compared an immune checkpoint inhibitor (avelumab, pembrolizumab or nivolumab) plus a tyrosine kinase inhibitor (TKI) (axitinib, cabozantinib or lenvatinib) with sunitinib as first-line treatment of RCC and shown improved PFS and/or OS.[38–41] The survival results are remarkably similar (table 2; figure 3).

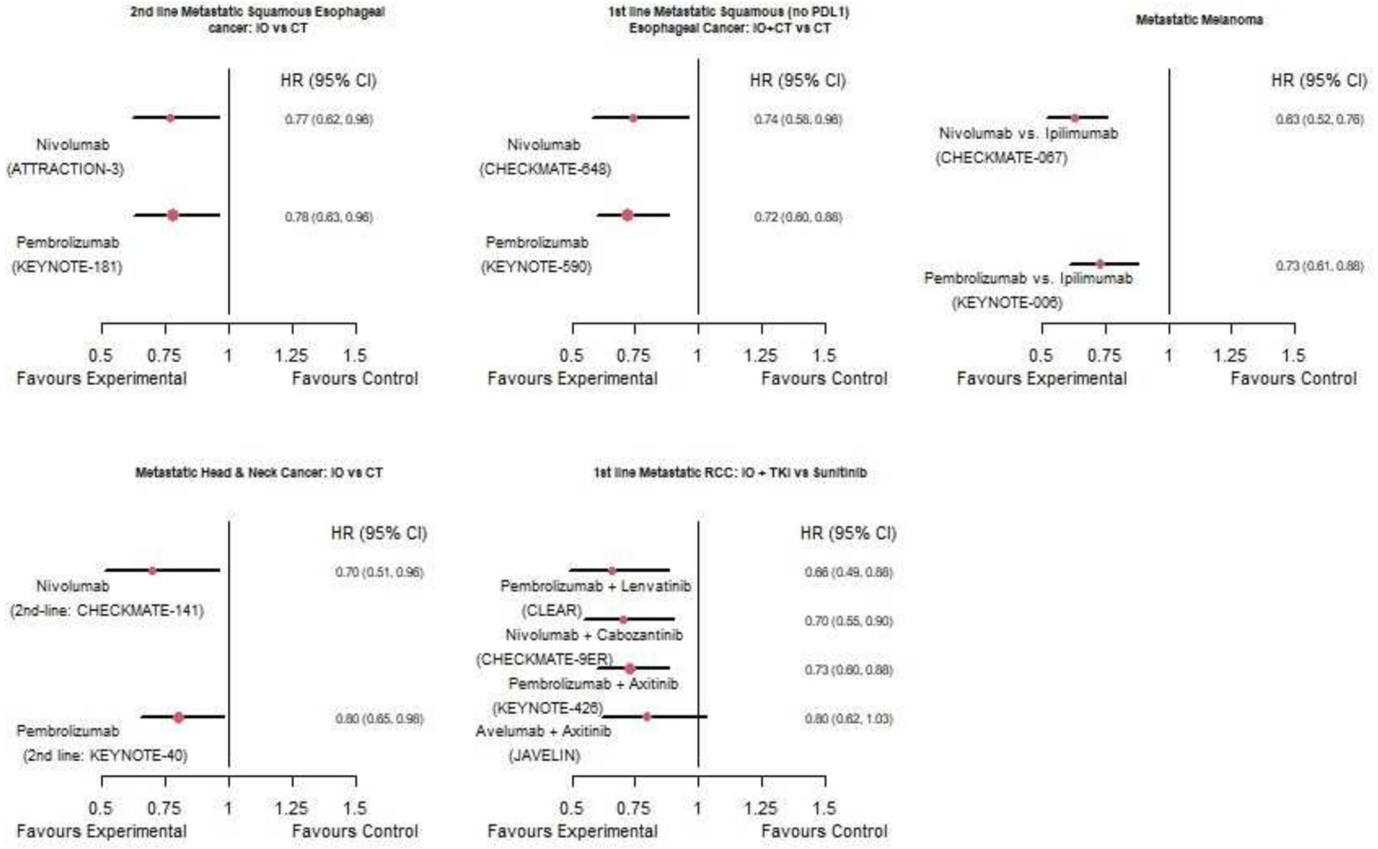

Figure 3 Forest plots of drug classes in oesophageal cancer, melanoma, head and neck and kidney cancer. CT, chemotherapy; IO, immunotherapy; TKI, tyrosine kinase inhibitor.

Immune checkpoint inhibitors

Four monoclonal antibodies that target the programmed death receptor PD-1 are approved by the FDA: nivolumab and pembrolizumab are in wide clinical use, while cemiplimab and dostarlimab have a limited spectrum of approval. Other drugs targeting PD-1 are in development. The crystal structures of the approved drugs and their binding sites on PD-1 are similar but not identical for pembrolizumab and nivolumab.[42 43] Three inhibitors of PD-L1, the ligand of PD-1, are approved and used clinically (atezolizumab, avelumab and durvalumab). These drugs also have similar but non-identical binding to their target.[42 43] PD-1 and PD-L1 inhibitors are approved by the FDA and EMA for treatment of different states of progression of many cancers, both as monotherapy and in combination with other drugs, and sometimes dependent on PD-L1 score, which quantifies expression of PD-L1 on tumour cells and infiltrating lymphocytes. There have been no head-to-head comparisons of these drugs in RCTs that might provide level 1 evidence of a class effect, and given the lack of motivation by sponsors for such trials, we can realistically assume that they will never be done. Available cross-comparisons of RCTs evaluating their use in similar clinical scenarios are summarised in table 2 and in figures 2 and 3. Most results of trials using different checkpoint inhibitors in similar clinical situations have given similar results, thereby providing support for a class effect. The limited exceptions appear attributable to subtle differences in design and conduct of the trials or to statistical variation in trial results that would be expected if any of them were repeated. The possibility of meaningful efficacy differences appears remote.

TOXICITY DIFFERENCES

There are sometimes different toxicity profiles among drugs within a class, even when efficacy appears to be similar. For example, unlike other androgen receptor inhibitors, darolutamide does not cross the blood–brain barrier, and perhaps should be the preferred drug in patients with a history of seizures. Ribociclib appears to cause more QT prolongation than the other CDK4/6 inhibitors palbociclib and abemaciclib, and perhaps should be avoided in patients with a history of cardiac disease. These differences in toxicity do not exclude definition of a class effect. Rather, some patients should not be considered for drug substitution. Thus, for men with prostate cancer, a class effect would allow the payer to decide which androgen receptor inhibitor should be used, except for the rare patient with a history of seizures. Also, some patients may develop a drug-specific toxicity and may need to be prescribed another drug within the class. An example could be an infusion reaction that

develops with cetuximab, and thus the need to transfer to panitumumab. These approaches would achieve two important goals—enabling clinically appropriate medical care, with substantial cost reduction for most patients.

DRUG PRICING: A POLICY PROPOSAL

Many anticancer drugs have similar efficacy to others in a class but this has not led to price competition in most countries, particularly in the USA; pricing of new drugs is set at a very similar level to competitors of the same class.[44–46] However, substantial price reductions are obtained when national authorities negotiate with companies for approval of their drugs to be funded by public health services, such as with the National Health Service of the UK. The Inflation Reduction Act in the USA will allow future negotiations between Medicare and pharmaceutical companies to lower drug prices, although anticancer drugs are not among those selected for initial negotiation.[47] It is likely that price reductions could also be obtained if national or subnational groups with high purchasing power negotiated with companies to provide preference (with defined exceptions) for use of a drug within a given class within their jurisdiction.

Additional policy manoeuvres are required to stimulate price competition, and we propose the following:

1. In different regions of the world, round table panels with both payers and providers be created to define potential class effects in different fields of oncology.
2. The panels should discuss drugs and classes in specific diseases.
3. The panels should define subgroups of patients, for whom a declared class effect would not apply.
4. The panels should discuss toxicities that would justify transferring between drugs within a class.
5. Once decisions are agreed between payers and providers regarding specific drug classes and clinical scenarios, payers would be free to negotiate with manufacturers regarding price. Following such negotiations, clear details should be distributed to the clinical community regarding which drugs are preferred.
6. To reduce confusion and bureaucracy among clinicians, the price negotiating process should occur infrequently—perhaps every 3 years for a specific indication.
7. In single-payer systems, this should be a relatively simple process. In multipayer systems (such as the USA), a national consortium could be created to define relevant drug classes, following which, individual payers could negotiate with manufacturers separately.

CONCLUSIONS AND FUTURE CONSIDERATIONS

There is considerable evidence to support class effects and therapeutic interchangeability among several families of anticancer drugs. These classes should be reviewed by payers and providers, leading to tendering processes to gain substantial price discounts. This process can lead to major reductions in financial toxicity, both at a society and individual level.

Anecdotal reports suggest that such approaches can lead to discounts of up to 30%, and from a health system perspective, this can translate to many millions of Euros or dollars. Until now, price negotiation on the basis of class effects has rarely been undertaken for cancer drugs, although the Norwegian healthcare system has adopted such an approach.[48] In Norway, there is a process similar to our policy proposal, where payers and providers meet in order to develop consensus about how to find the most appropriate solution, in order to satisfy the needs of all stakeholders. The opportunity to exploit class effects in oncology should be explored more deeply by healthcare systems around the world.

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ORCID iD

Ian F Tannock http://orcid.org/0000-0002-2636-7041

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