Beyond The Guidelines: Urologic Oncology Investigators Provide Perspectives on the Optimal Management of Urothelial Bladder Cancer

Clinical Investigator Survey

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Urothelial Bladder Cancer Survey Respondents

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MODULE 1: Current Role of Anti-PD-1/PD-L1 Antibodies in the Treatment of Non-Muscle-Invasive Bladder Cancer (NMIBC)

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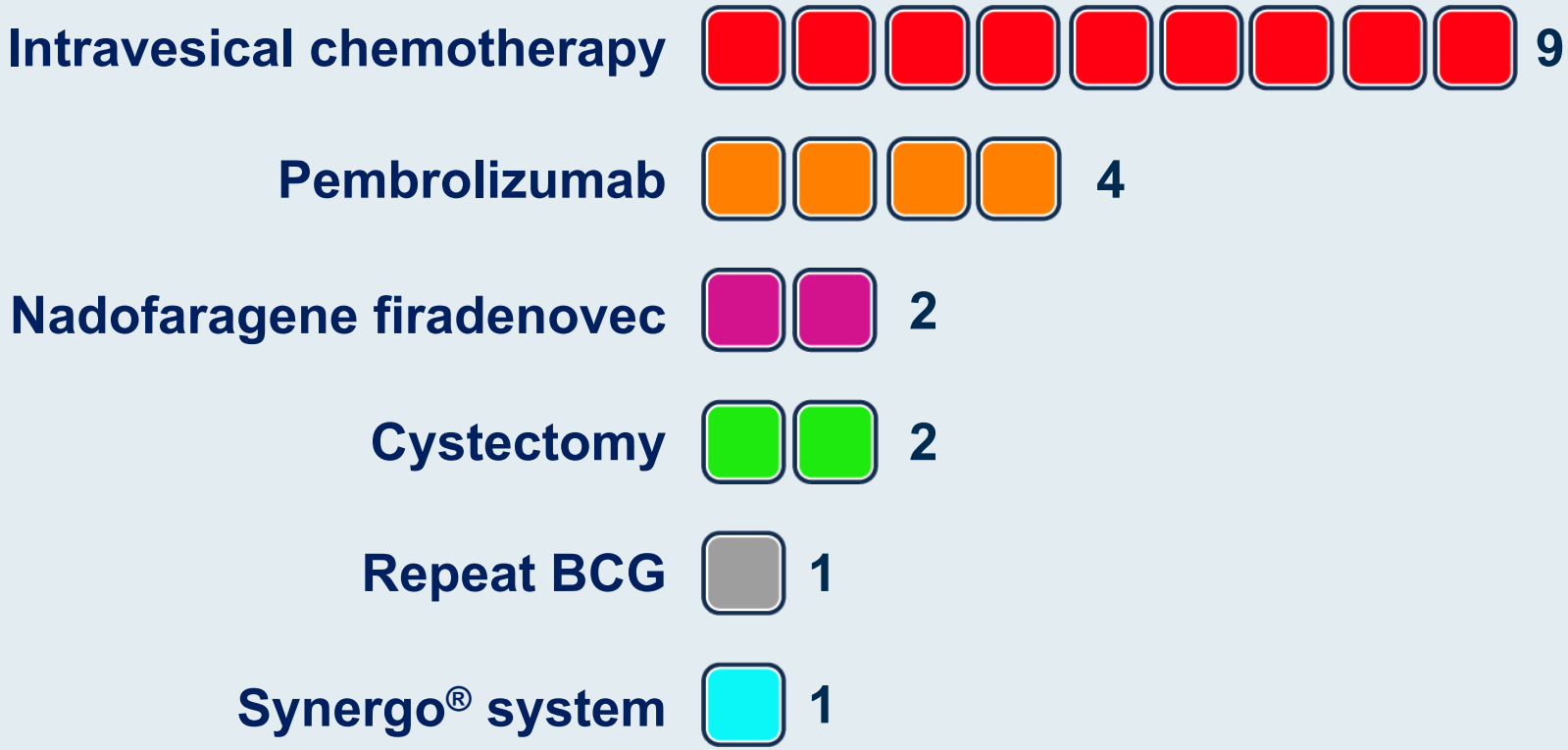
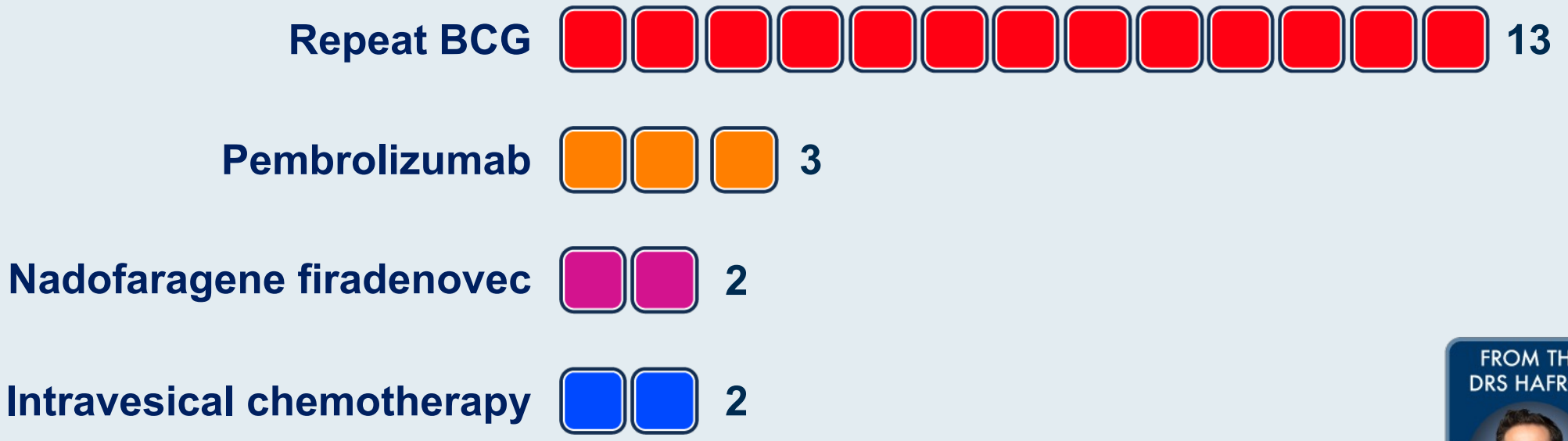
An 83-year-old man undergoing evaluation for hematuria is noted to have erythematous patches on cystoscopy. Biopsy confirms carcinoma in situ (CIS) in a diffuse pattern. Complete resection or fulguration is impossible because of the extent of disease. He receives BCG induction x 6 with maintenance for 18 months before recurrence is noted on cystoscopy. Biopsy confirms CIS recurrence. Regulatory and reimbursement issues aside, what would you recommend?



Survey of urologic oncology clinical investigators

A 59-year-old man presented with hematuria and underwent TURBT with gemcitabine, which showed high-grade T1 urothelial bladder cancer (UBC) without muscle present in the specimen. A CT urogram was negative. Repeat transuretheral resection 6 weeks later shows CIS with muscle present in the specimen. The patient receives induction BCG x 6. At the 3-month post-BCG cystoscopy, cytology is positive but an office cystoscopy is negative. Additional biopsies demonstrate CIS at the dome of the bladder. The patient refuses cystectomy. Regulatory and reimbursement issues aside, what would you recommend?



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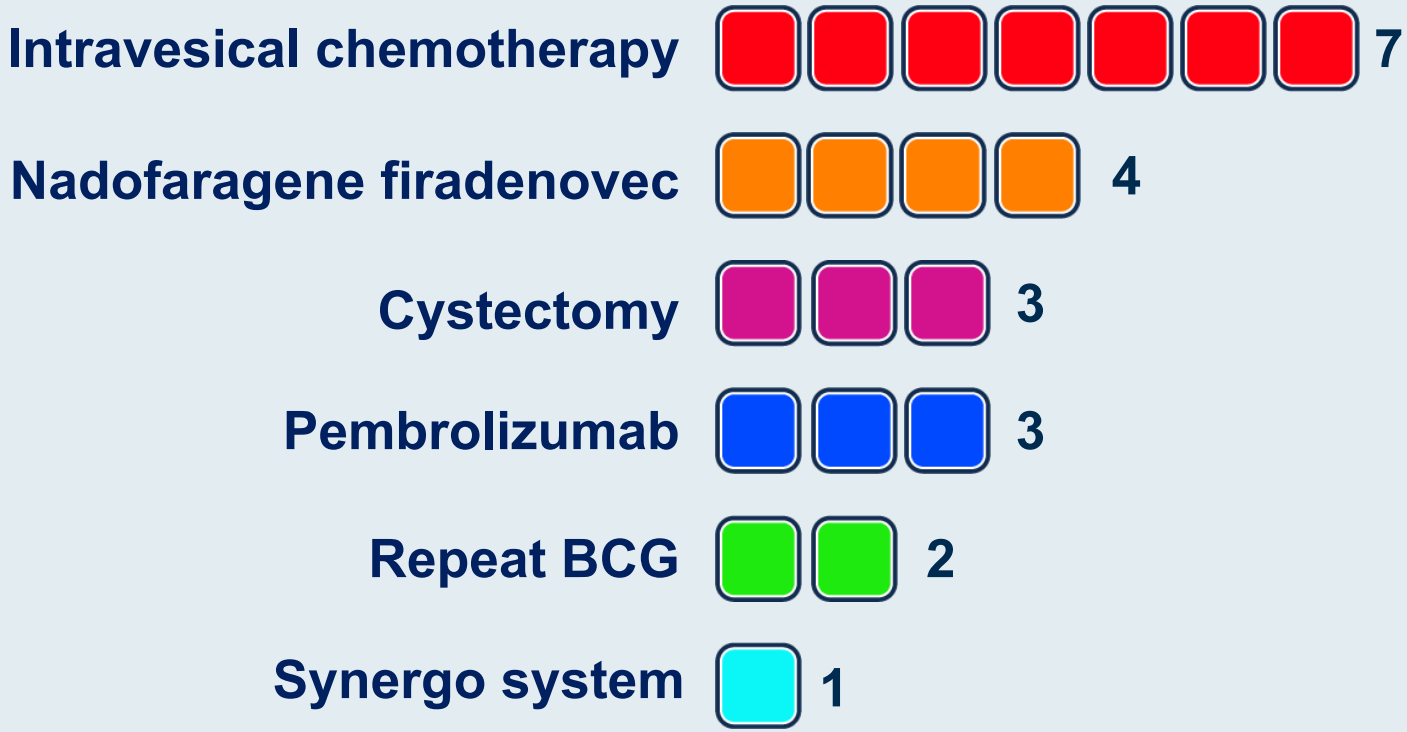
A 64-year-old man presents with asymptomatic gross hematuria. Cystoscopy reveals an erythematous area on the posterior bladder wall and a 1-cm papillary tumor on the right lateral wall. TURBT shows CIS on the posterior bladder wall and high-grade pTa disease on the right lateral wall. The patient completes induction BCG x 6 followed by 6 months of maintenance BCG. The 9-month cystoscopy indicates erythema on the right hemitrigone/posterior wall. Biopsy demonstrates recurrent CIS. Regulatory and reimbursement issues aside, what would you recommend?



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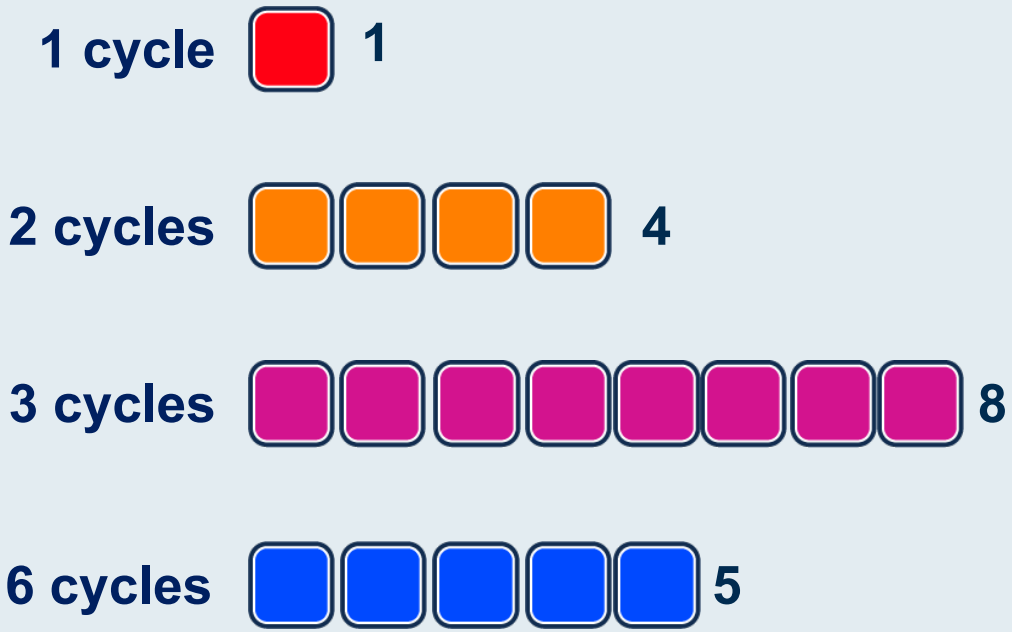
For a patient with BCG-unresponsive non-muscle-invasive UBC (NMIBC) who is receiving pembrolizumab, how many cycles of therapy would you administer without a clinical response before you switched to an alternative treatment?



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To what extent has the ongoing shortage of BCG affected your practice?

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MODULE 2: Contemporary Management of Muscle-Invasive Bladder Cancer (MIBC)

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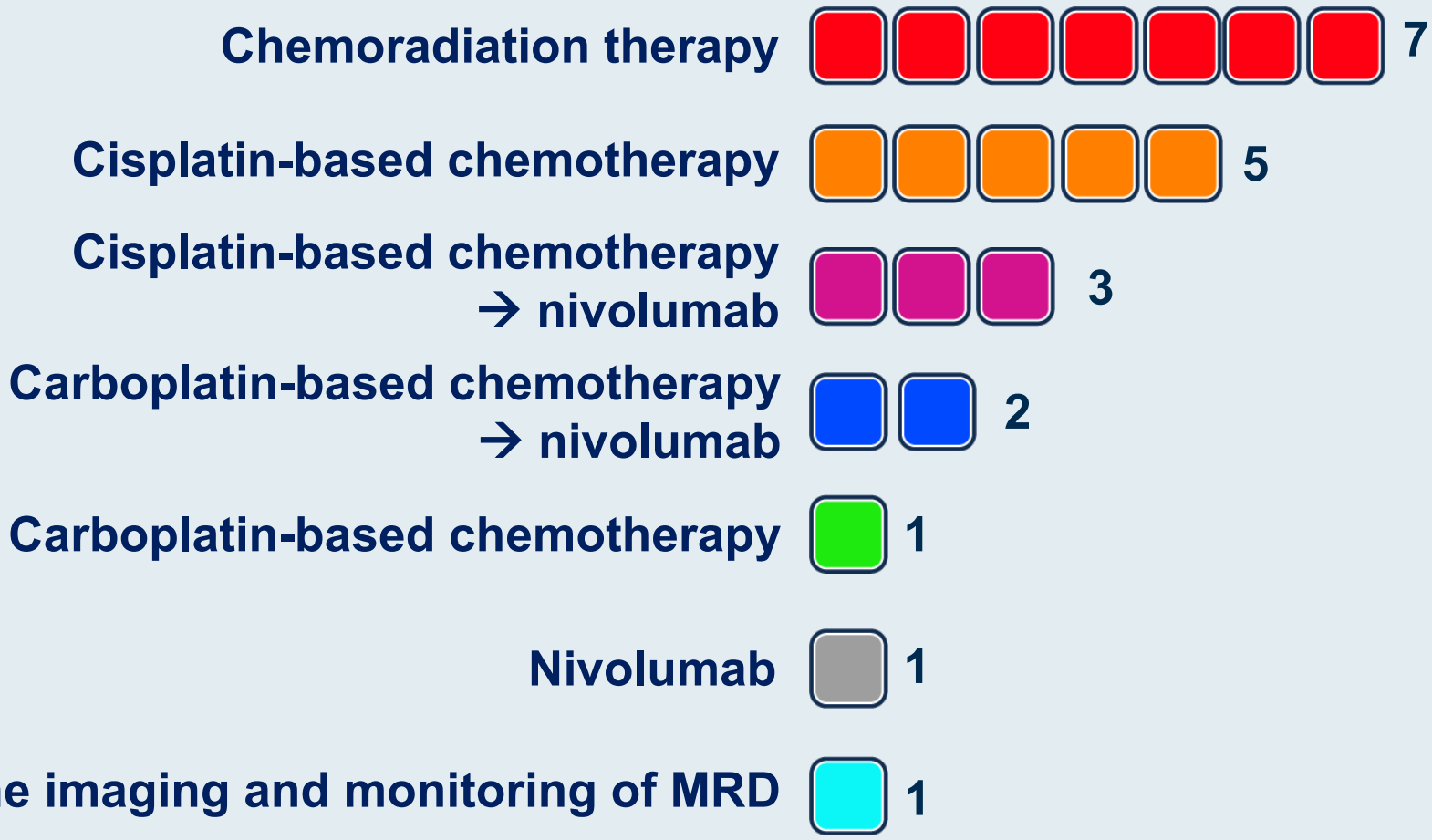
An 84-year-old morbidly obese man with diabetes mellitus, mild neuropathy and a glomerular filtration rate (GFR) of 50 undergoes evaluation for hematuria and a large mass is found and shown to be T2 UBC on maximal resection. He refuses cystectomy and requests a bladder-sparing approach. Regulatory and reimbursement issues aside, which treatment would you recommend?



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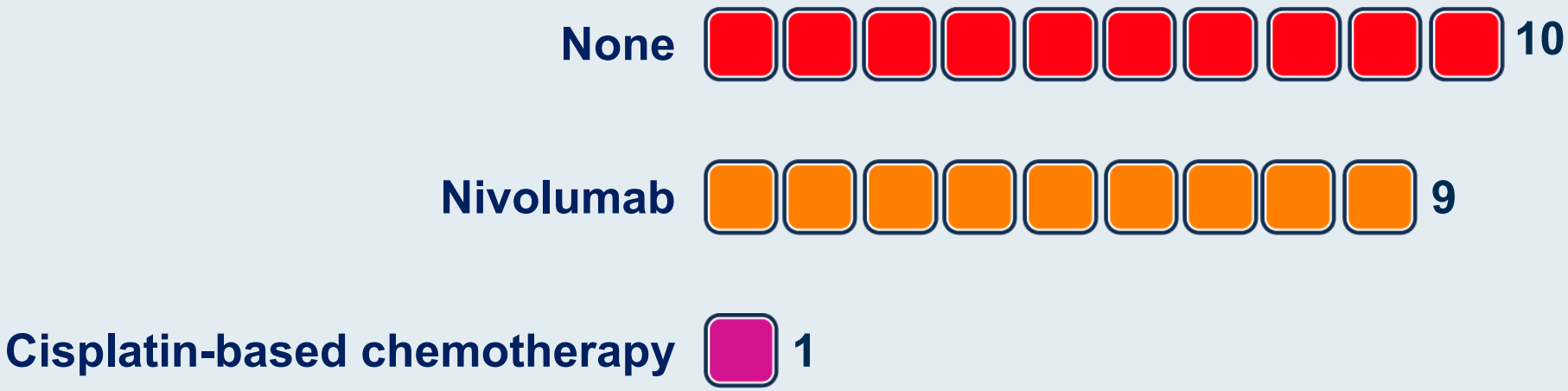
A 74-year-old man presents with a history of hematuria, and office cystoscopy shows a large papillary lesion. He undergoes TURBT, which shows T2 transitional cell carcinoma (TCC), and receives neoadjuvant chemotherapy with gemcitabine/cisplatin followed by robotic cystectomy with ileal conduit. Pathology reveals pT2apN0 with negative margins. Regulatory and reimbursement issues aside, which adjuvant systemic therapy, if any, would you recommend?



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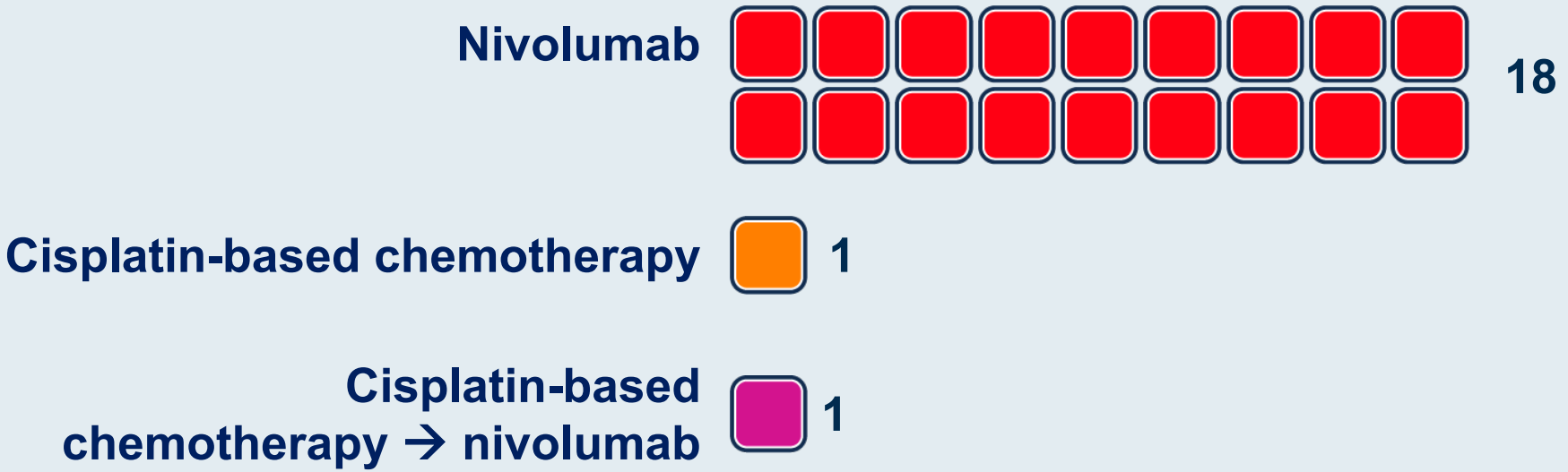
An 84-year-old man presents with a 4-cm bladder mass consistent with T2 UBC. Metastatic evaluation is negative. He receives neoadjuvant chemotherapy with gemcitabine/cisplatin followed by robotic cystectomy with ileal conduit. Pathology reveals T3aN1 and 2/16 positive lymph nodes. Regulatory and reimbursement issues aside, which adjuvant systemic therapy, if any, would you recommend?



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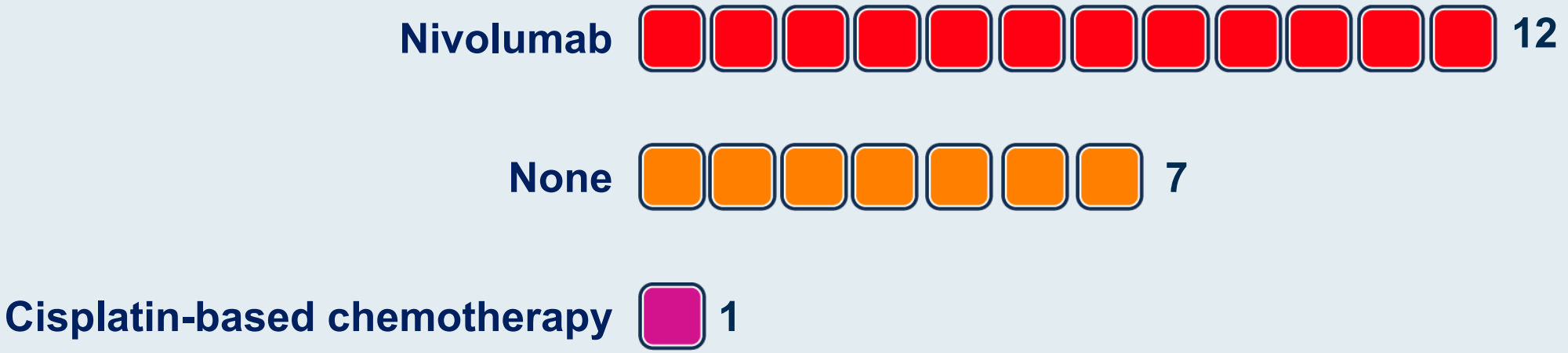
A 67-year-old woman with pT2 UBC and hydronephrosis, suggesting cT3 disease, receives neoadjuvant gemcitabine/cisplatin x 6 and undergoes cystectomy with residual T2 disease. Regulatory and reimbursement issues aside, which adjuvant systemic therapy, if any, would you recommend?



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MODULE 3: Novel Strategies Under Investigation for Nonmetastatic Urothelial Bladder Cancer (UBC)

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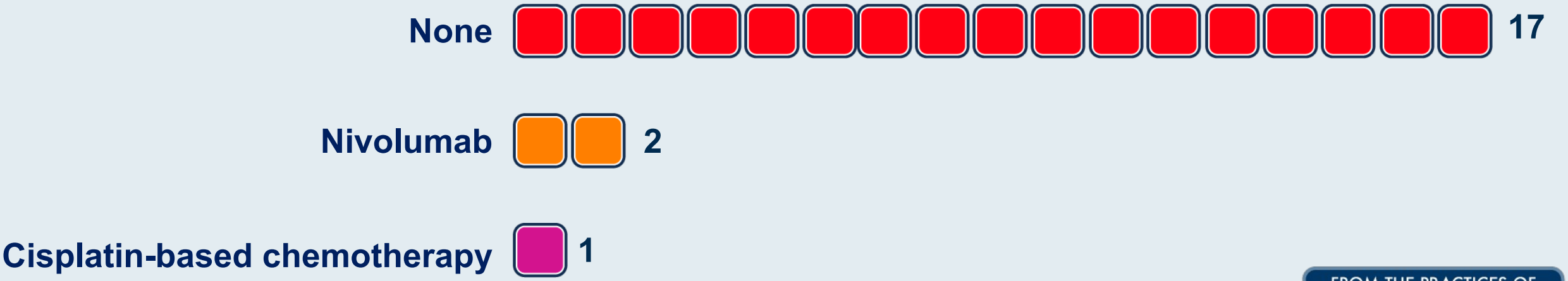
A 57-year-old woman presents with gross hematuria and is found to have T2 bladder TCC. CT scan of chest, abdomen and pelvis is negative. She receives neoadjuvant gemcitabine/cisplatin followed by robotic cystectomy with neobladder construction. Pathology reveals pT0N0 and 0/21 positive lymph nodes. Regulatory and reimbursement issues aside, which adjuvant systemic therapy, if any, would you recommend?



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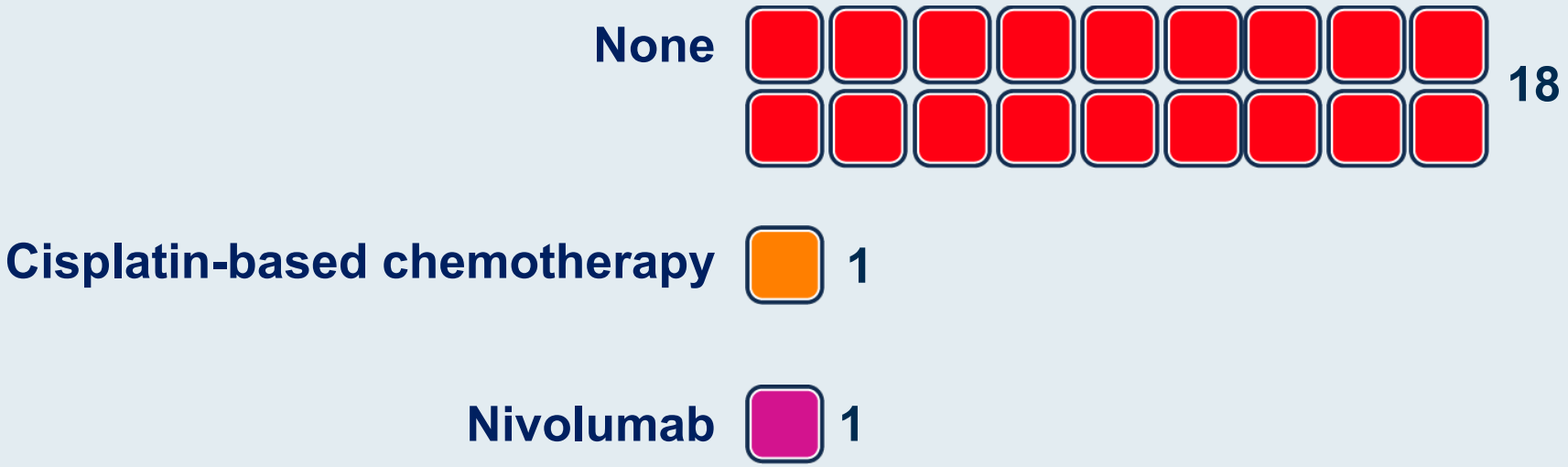
A 60-year-old man presents with microhematuria and dysuria. He undergoes cystoscopy, which shows diffuse erythema of the bladder. Multiple biopsies are performed, and CIS is shown in 5/5 of the bladder biopsies. Cytology and FISH are positive. CT imaging of chest and abdomen are negative. He undergoes robotic cystectomy with neobladder construction. Pathology shows extensive pTispN0 and 0/9 positive lymph nodes. Regulatory and reimbursement issues aside, which adjuvant systemic therapy, if any, would you recommend?



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A 63-year-old man presents with hematuria and flank pain. CT evaluation reveals hydronephrosis and a renal mass at the ureteropelvic junction. No lymphadenopathy is noted. Cystoscopy with ureteroscopy shows an apparently high-grade tumor. He undergoes a biopsy that is nondiagnostic, cytology and washings with atypical cells. He elects nephroureterectomy. Final pathology reveals pT3 with invasion through the muscularis of the proximal ureter into perivesical fat. Negative margins. Regulatory and reimbursement issues aside, what would you most likely recommend?

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MODULE 4: Current and Future Up-Front Management of Metastatic UBC (mUBC)

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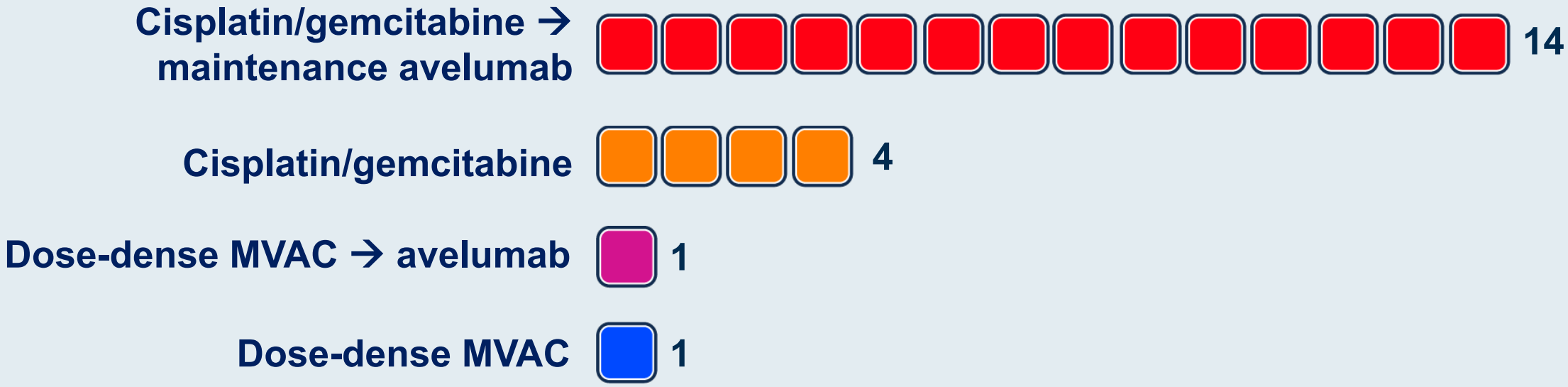
What would be your preferred first-line treatment regimen for a 65-year-old patient with metastatic UBC and no prior systemic treatment?



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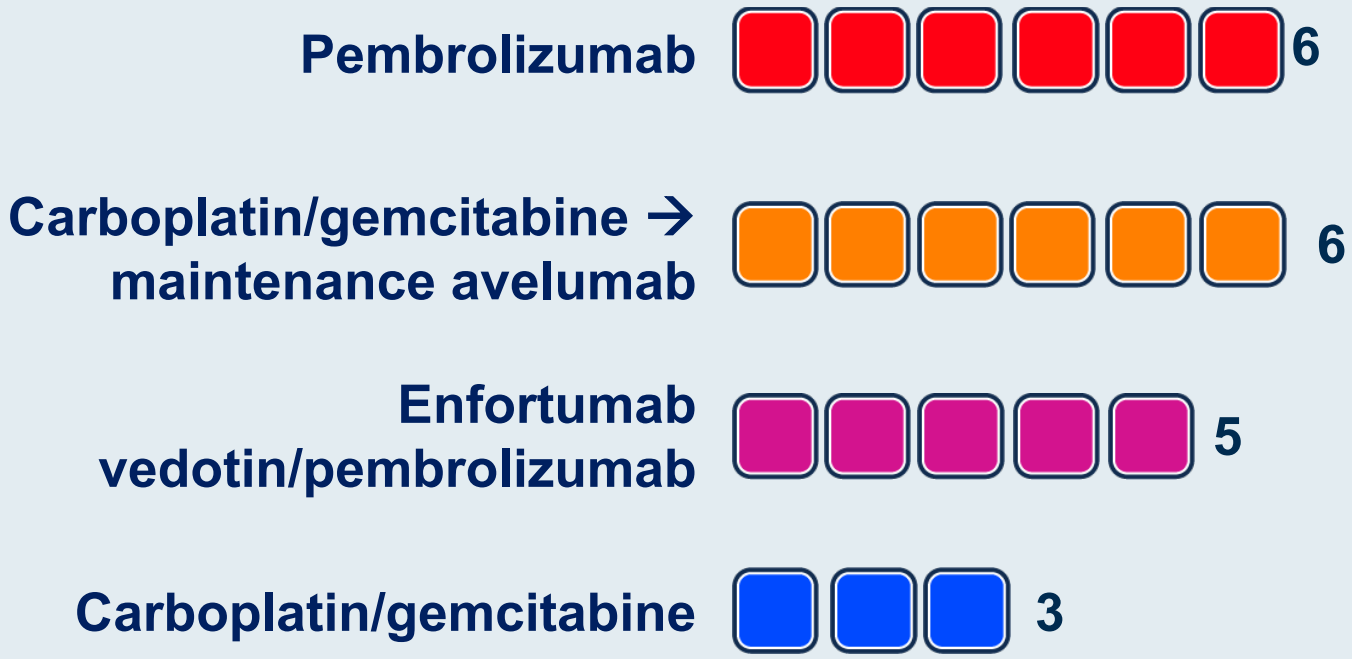
What would be your preferred first-line regimen for an 80-year-old patient with metastatic UBC and no prior systemic treatment who is not a candidate for cisplatin-based therapy?



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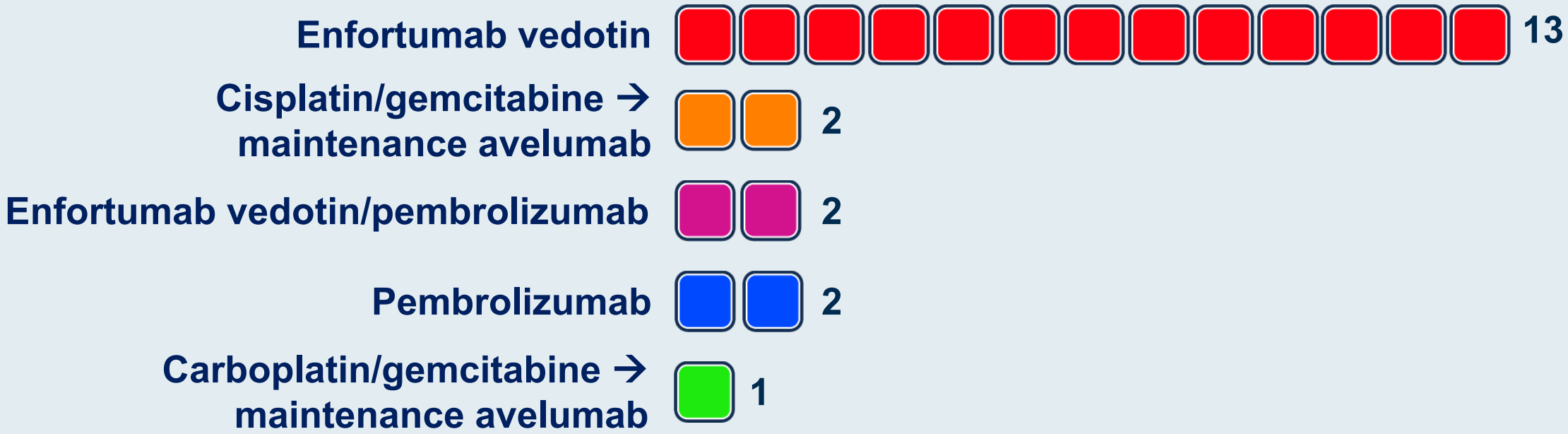
A 65-year-old patient receives neoadjuvant chemotherapy followed by cystectomy and then adjuvant nivolumab for FGFR wild-type UBC but develops metastatic disease 9 months after starting nivolumab. Regulatory and reimbursement issues aside, what would you likely recommend?



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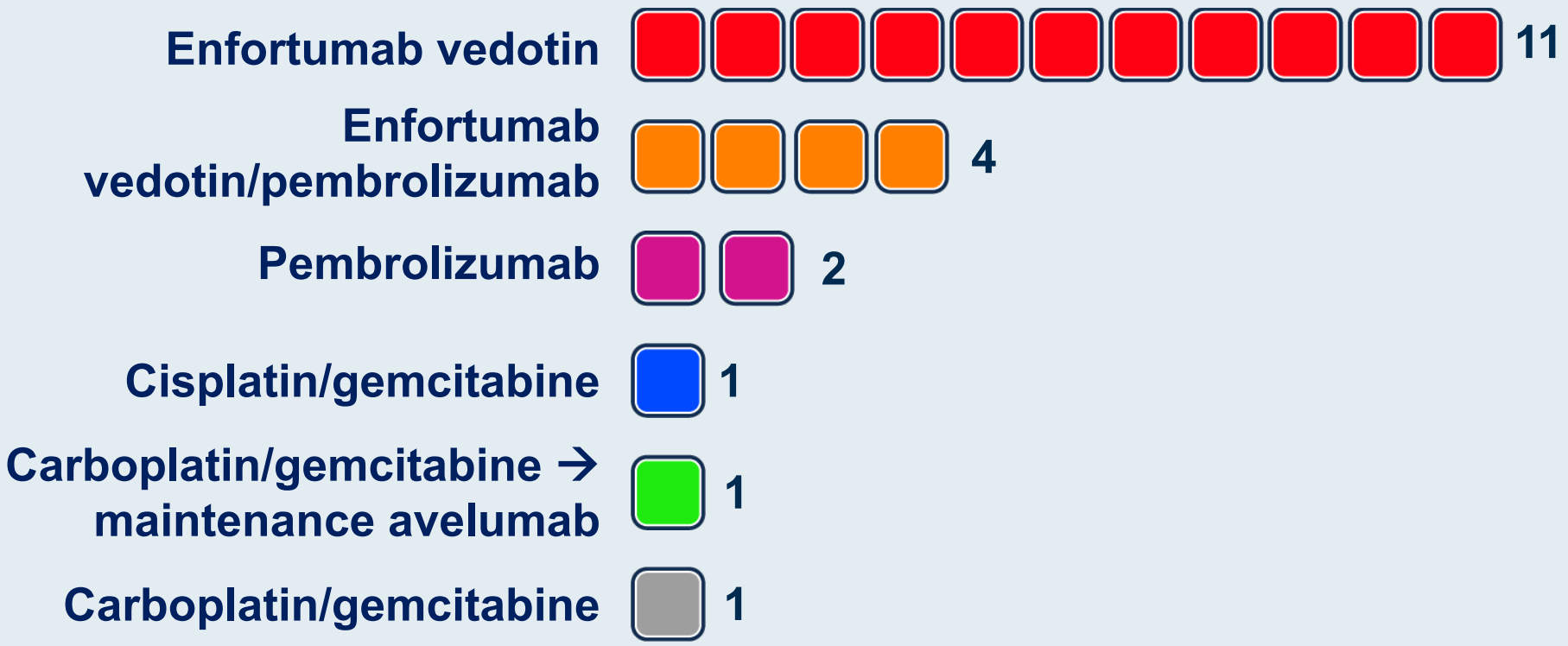
Regulatory and reimbursement issues aside, what would you generally recommend for an 80-year-old platinum-ineligible patient who undergoes cystectomy followed by adjuvant nivolumab for FGFR wild-type UBC but develops liver metastases 9 months after starting nivolumab?



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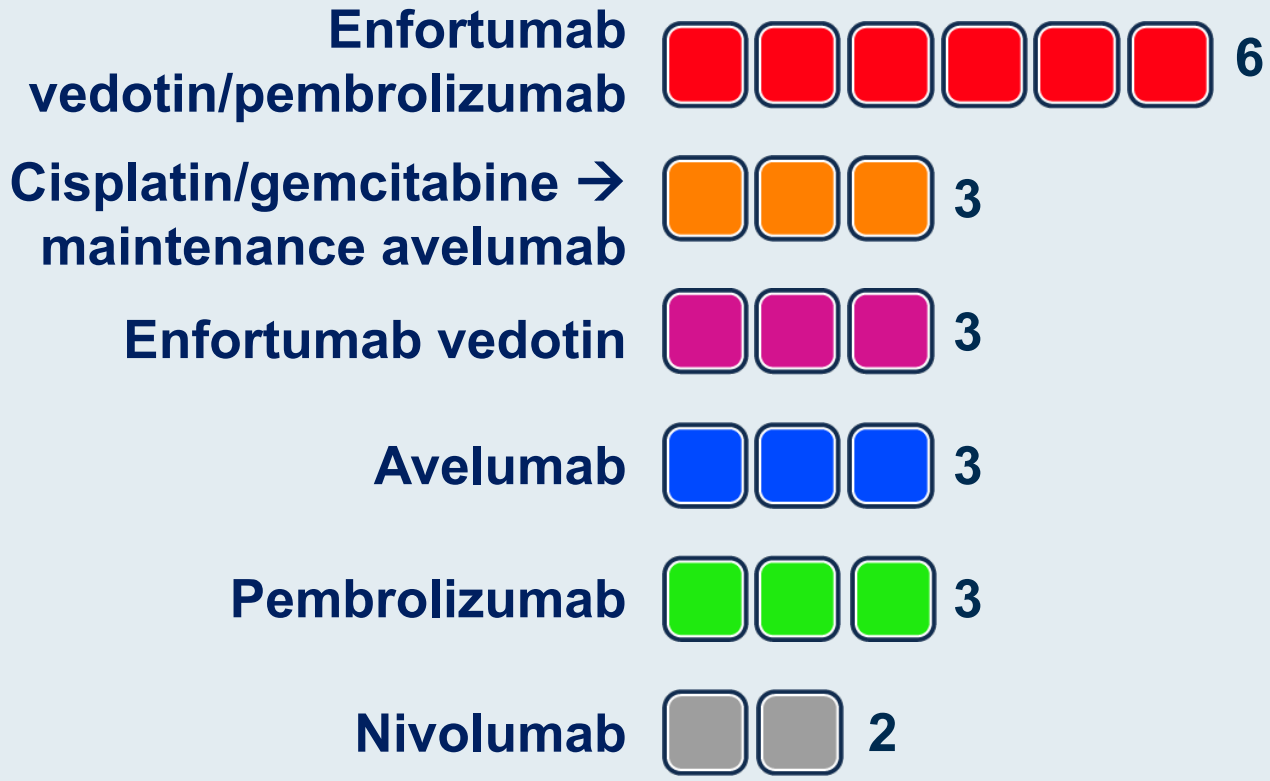
An 85-year-old woman underwent cystectomy for pT3N1 disease 3 years ago. She received adjuvant gemcitabine/cisplatin for nodal disease. ECOG PS is 0. Recent surveillance imaging reveals retroperitoneal lymphadenopathy and small lung nodules. FGFR wild type. Regulatory and reimbursement issues aside, what would be your preferred first-line therapy?



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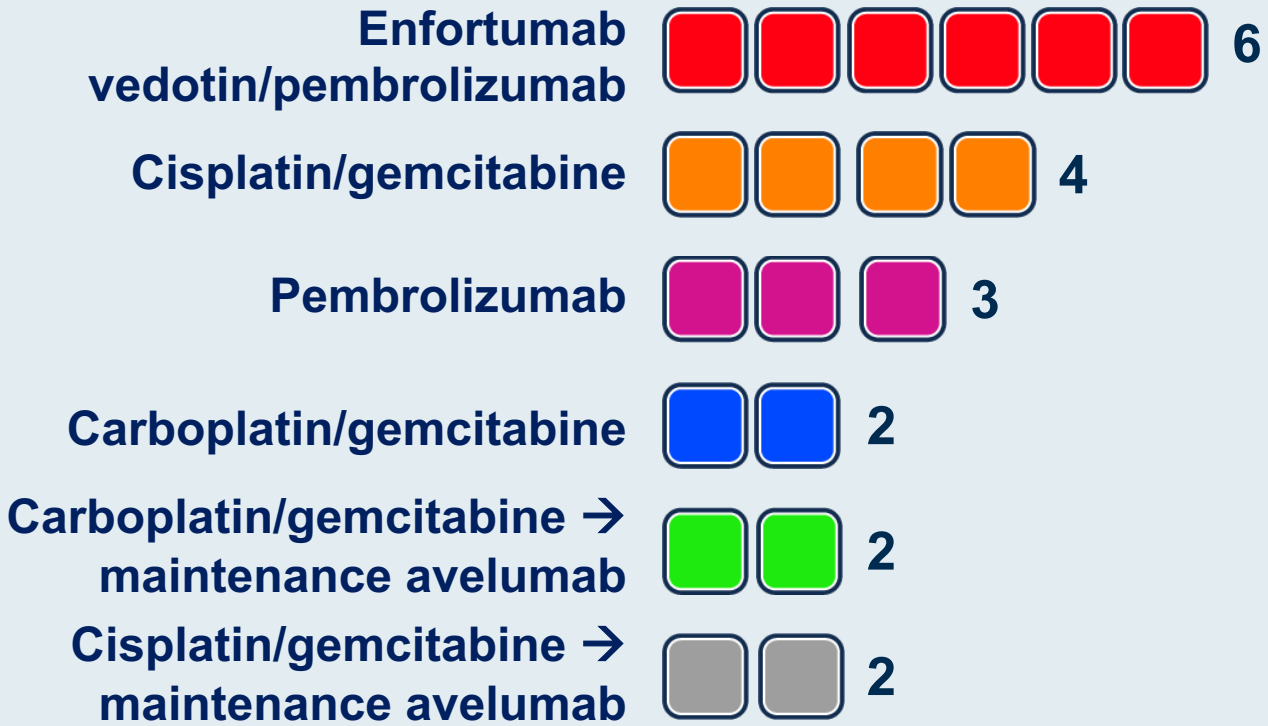
An 81-year-old man undergoes evaluation for hematuria, and a large bladder mass is noted on abdominal/pelvic CT. Initial TURBT confirms high-grade UBC with no muscle in the specimen. Resection is incomplete because of the large tumor size. Clinical stage is T2 based on the CT imaging. FDG-PET imaging reveals multiple lung nodules. GFR is 40. Regulatory and reimbursement issues aside, what would be your preferred first-line therapy?



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MODULE 5: Selection and Sequencing of Therapy for Relapsed/Refractory mUBC

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A 65-year-old patient receives neoadjuvant chemotherapy followed by cystectomy and then adjuvant nivolumab for FGFR-mutated UBC but develops metastatic disease 9 months after starting nivolumab. Regulatory and reimbursement issues aside, what would you likely recommend?

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Regulatory and reimbursement issues aside, what would you generally recommend for an 80-year-old platinum-ineligible patient who undergoes cystectomy followed by adjuvant nivolumab for FGFR-mutated UBC but develops liver metastases 9 months after starting nivolumab?

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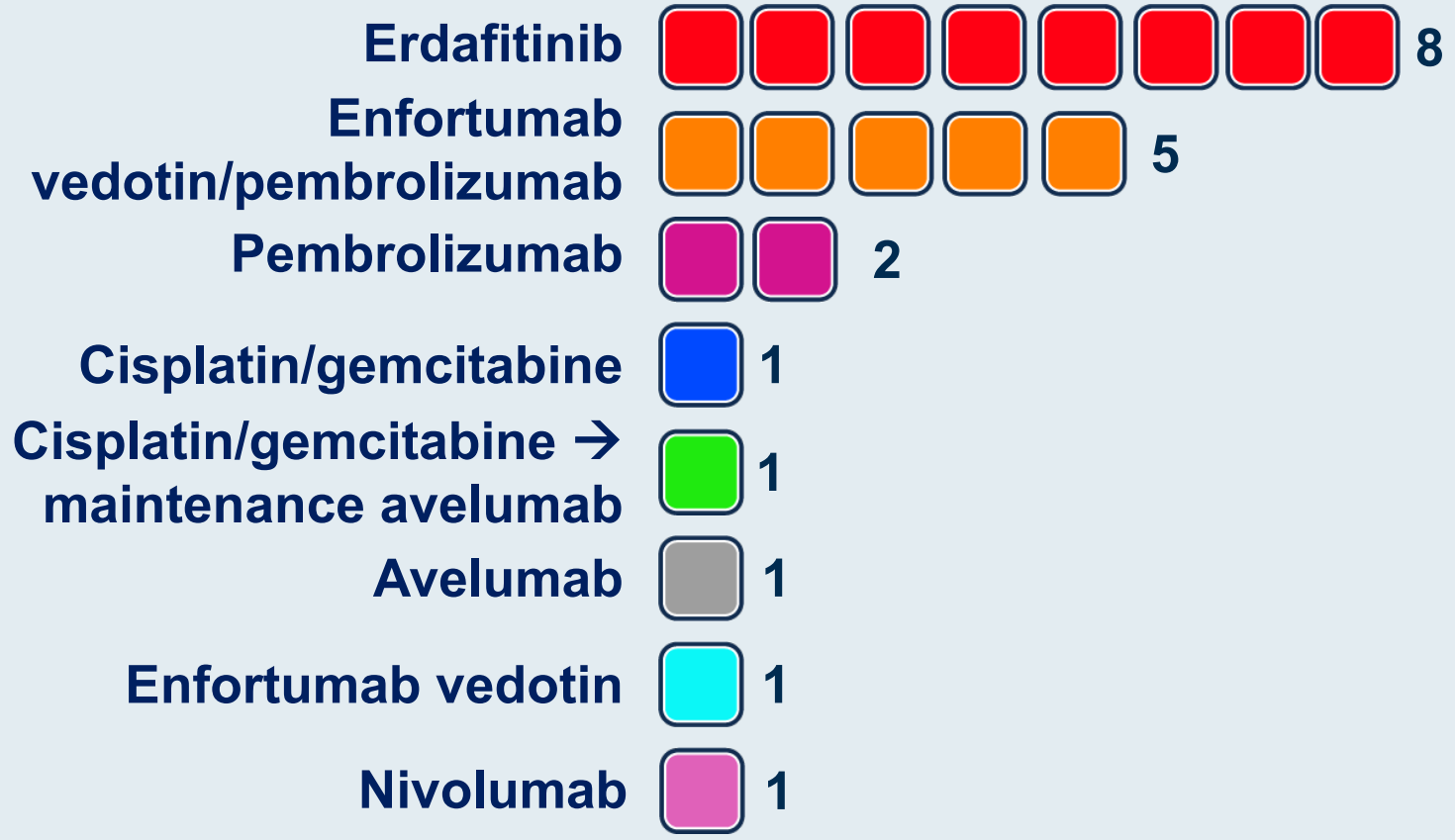
An 85-year-old woman underwent cystectomy for pT3N1 disease 3 years ago. She received adjuvant gemcitabine/cisplatin for nodal disease. ECOG PS is 0. Recent surveillance imaging reveals retroperitoneal lymphadenopathy and small lung nodules. FGFR mutated. Regulatory and reimbursement issues aside, what would be your preferred first-line therapy?



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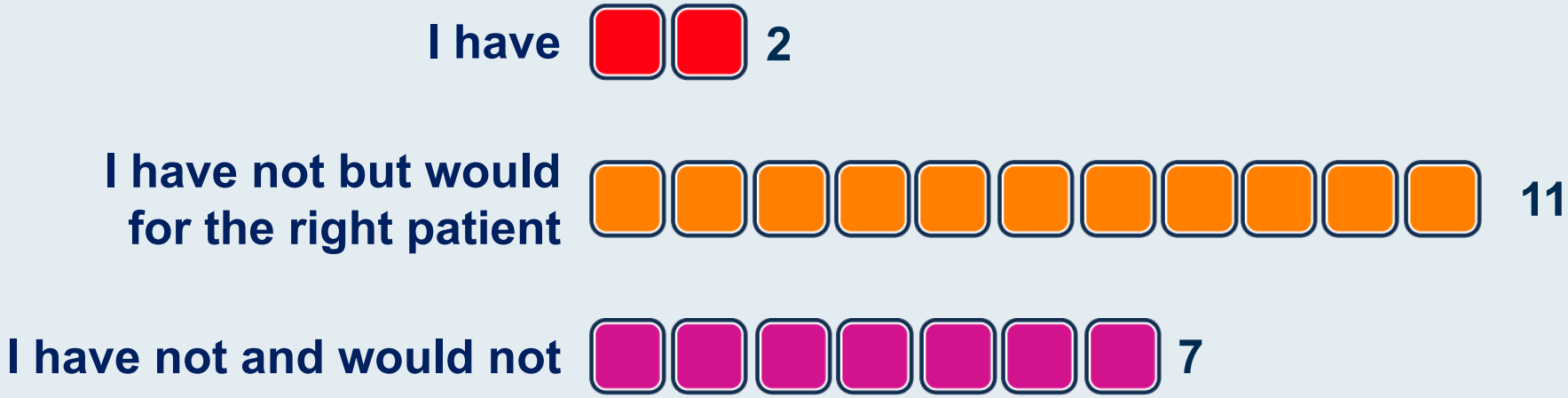
Do you generally conduct HER2 testing for your patients with metastatic UBC?

Have you offered or would you offer HER2-targeted therapy to your patients with HER2-positive metastatic UBC outside of a protocol setting?



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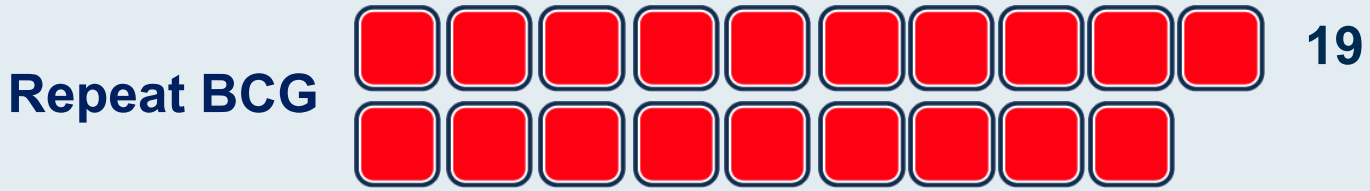
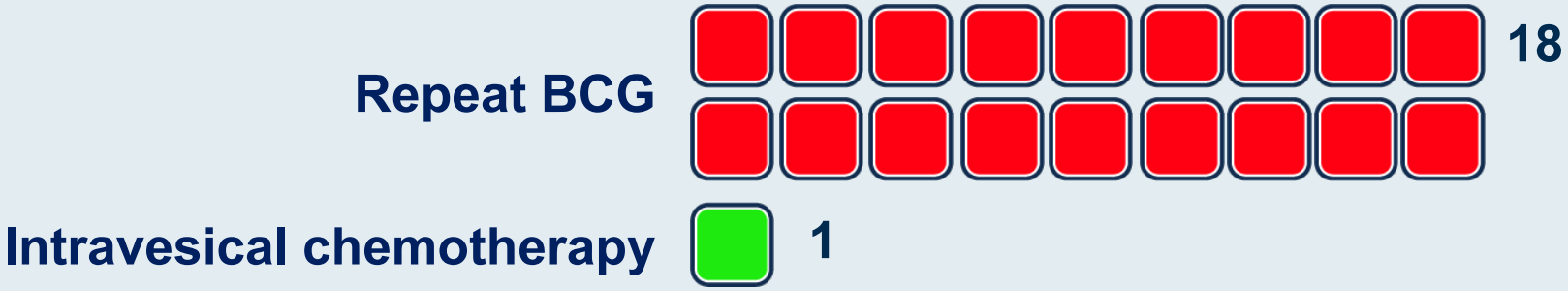
Additional Survey Findings

A 78-year-old man with a history of high-grade Ta urothelial UBC receives BCG induction therapy x 6 but no maintenance BCG. He has been under surveillance and now has noted recurrence with confirmed high-grade disease. Regulatory and reimbursement issues aside, what would you recommend if the patient had originally undergone resection…

Five years ago



One year ago



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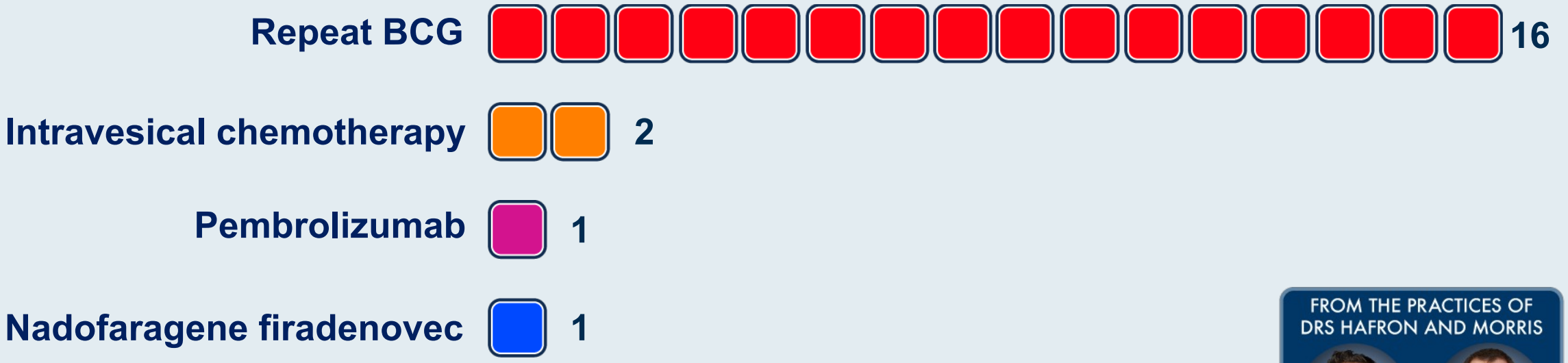
A 72-year-old man received treatment for UBC 5 years ago by an outside urologist. Pathology at that time showed high-grade T1 UBC, and he underwent TURBT only. He now presents with gross hematuria, and office cystoscopy shows a 1.5-cm papillary lesion on the left lateral wall. TURBT with intravesical gemcitabine shows a high-grade Ta lesion with muscle present. The patient receives induction BCG x 6. Surveillance 12-month cystoscopy shows carcinoma in situ (CIS) at the dome of the bladder. Regulatory and reimbursement issues aside, what would you recommend?



FROM THE PRACTICES OF DRS HAFRON AND MORRIS

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At what point, if any, would you consider a checkpoint inhibitor for the patient in the previous scenario?

- I would not
- After bcg and intravesicle chemo if not a cystectomy candidate
- He needs more maintenance
- Would not consider here
- After BCG induction x 2 and IV chemo failure
- When BCG unresponsive
- Not approved in Europe; only if I have a trial
- Persistence following additional BCG with maintenance, and refusal of cystectomy
- Failed BCG x 2
- I wouldn't, as data not impressive and costly med for 12-mo CR 19%
- In context of clinical trial
- If he recurs after a maintenance course of BCG
- Failure of BCG 5/6 induction and 2/3 maintenance
- After 2 induction courses or after 1 induction course and 1 course of gemcitabine/docetaxel
- Would not consider CPI — gemcitabine/docetaxel much better
- Only if he were to be nonresponsive to a 2nd induction round of BCG
- After adequate BCG and salvage intravesical gemcitabine/docetaxel

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If you decided to use a checkpoint inhibitor for the patient in the previous scenario, which one would you use?

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A 78-year-old man with a significant medical history who is not a candidate for cystectomy is found to have high-grade Ta UBC on TURBT and receives induction BCG. On first cystoscopy 2 months after BCG completion, a recurrent mass is noted. TURBT shows high-grade T1 with CIS. Regulatory and reimbursement issues aside, what would you recommend?

FROM THE PRACTICES OF DRS HAFRON AND MORRIS

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A 71-year-old man presented 3 years ago with high-grade T1 transitional cell carcinoma (TCC) of the bladder and received BCG induction x 6. Upper tract imaging is negative. The 3-month follow-up cystoscopy reveals recurrent CIS. The patient refuses cystectomy and undergoes a second course of BCG x 6 without maintenance. The 9-month post-treatment cystoscopy shows CIS recurrence. Regulatory and reimbursement issues aside, what would you recommend?

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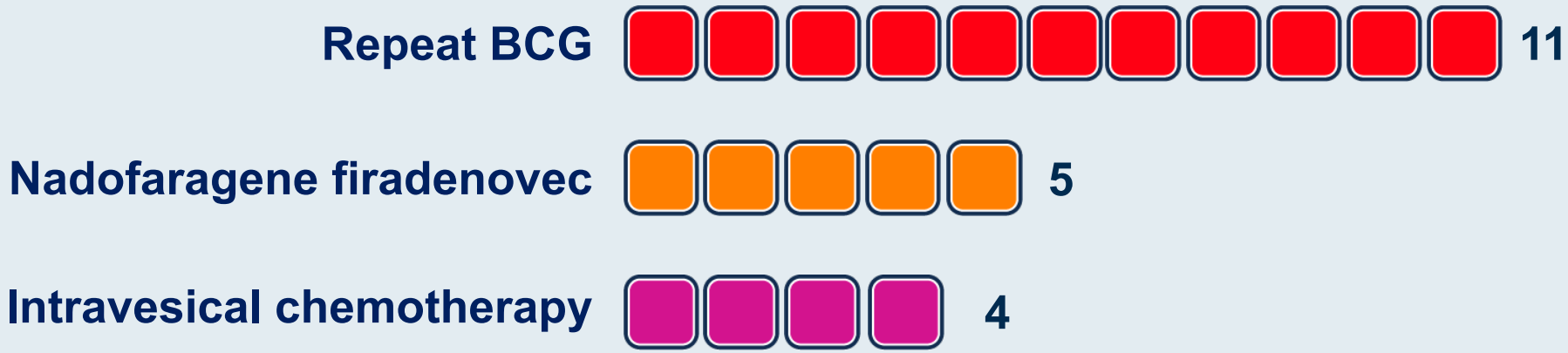
An 85-year-old man with cardiovascular comorbidities presented with hematuria and underwent TURBT with gemcitabine, which showed high-grade T1 UBC without muscle present in the specimen. A CT urogram was negative. Repeat transuretheral resection 6 weeks later shows CIS with muscle present in the specimen. The patient receives induction BCG x 6. At the 3-month post-BCG cystoscopy, cytology is positive but an office cystoscopy is negative. Additional biopsies demonstrate CIS at the dome of the bladder. The patient is not considered a cystectomy candidate. Regulatory and reimbursement issues aside, what would you recommend?



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A 76-year-old man is diagnosed with high-grade CIS and completes induction BCG x 6. The 6-month post-BCG cystoscopy shows recurrent CIS. The patient refuses cystectomy, and a second course of BCG x 6 is completed. Post-BCG biopsy is negative but with suspicious cytology. The 2-year post-BCG cystoscopy reveals CIS with suspicious cytology, and a retrograde pyelogram is negative. Regulatory and reimbursement issues aside, what would you recommend?

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How often do you perform follow-up cystoscopy for patients with BCG-unresponsive NMIBC who are receiving pembrolizumab?

Every 3 months for the first 2 years and every 6 months thereafter, as in the KEYNOTE-057 trial

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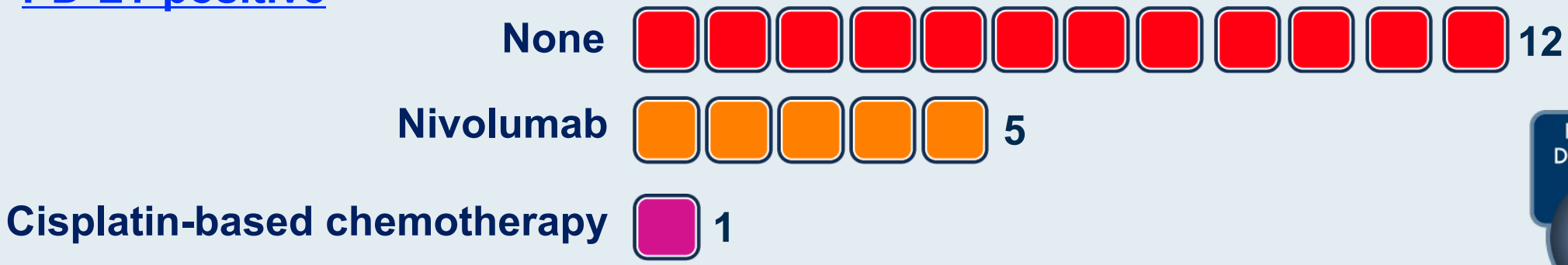
A 72-year-old woman with cT3 UBC receives neoadjuvant gemcitabine/cisplatin x 4 and undergoes cystectomy. Final pathology reveals pT2n0. The patient is concerned about toxicity from the recommended maintenance immunotherapy. ctDNA testing for minimally residual disease suggests no residual circulating tumor. Regulatory and reimbursement issues aside, which adjuvant systemic therapy, if any, would you recommend if the patient's tumor were…

PD-L1-negative

PD-L1-positive



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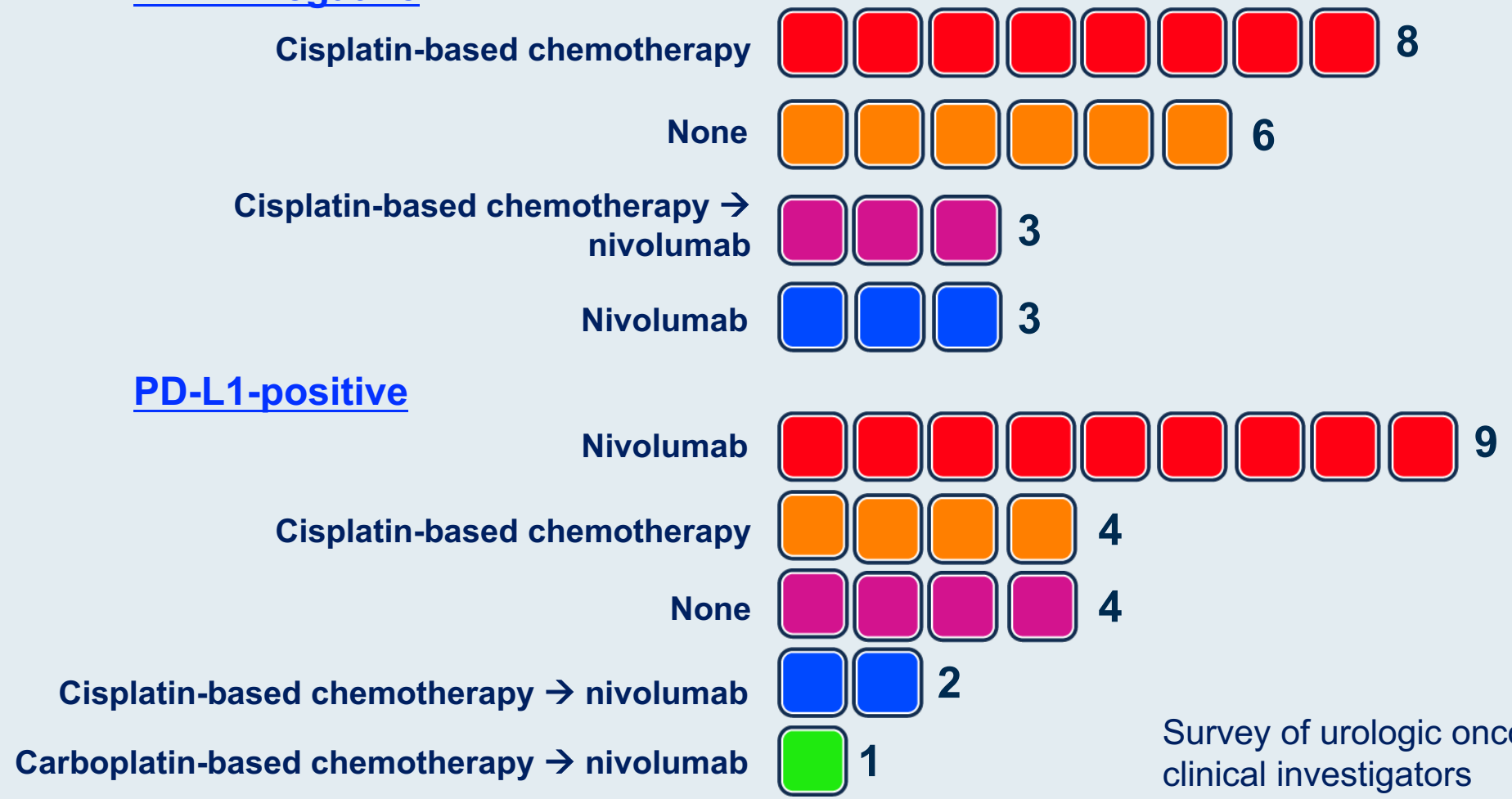
A 72-year-old woman presents from an outside hospital with TURBT showing squamous cell carcinoma of the bladder. CT demonstrates a 6.4-cm mass at the dome of the bladder. No lymphadenopathy. Robotic cystectomy with ileal conduit reveals high-grade invasive UBC with squamous differentiation. 5 pericystic reactive lymph nodes are negative for carcinoma (0/5). pT3bN0, negative margins. Regulatory and reimbursement issues aside, which adjuvant systemic therapy, if any, would you recommend if the patient's tumor were…



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