

Table 12.2 Examples of Antisense Oligonucleotides That Have Entered Clinical Trials

| mRNA Target | Antisense Oligonucleotide (Chapter/Section) | Evaluated Tumors |
|------------------|---|---------------------------|
| <i>PKC</i> | ISIS-3521 (LY-900003, Affinitac [®]) (10/5.4) | NSCLC, solid tumors |
| <i>RAS</i> | ISIS-2503 (10/6.1) | Solid tumors |
| <i>c-RAF</i> | ISIS-5132 (CGP-69846A) (10/6.5.1) | Solid tumors |
| <i>BCL-2</i> | Oblimersen (Genasense [®]) (11/8.1.3) | Melanoma, MM, CLL, NSCLC |
| <i>DNMT</i> | MG-98 (8/2.2) | Solid tumors |
| <i>hTR</i> | Imetelstat (GRN-163 L) (7/8.3) | MM, solid tumors |
| <i>Clusterin</i> | OGX-011 (Custirsen [®]) (11/8.2) | Lung and prostate cancers |
| <i>P53</i> | OL(1)p53 (11/8.1.4) | AML, MDS |
| <i>RRM2</i> | GTI-2040 (12/6) | CRPC |
| <i>c-MYB</i> | LR/INX-3001 (12/6) | CML |

7 BACTERIA AND BACTERIAL TOXINS IN CANCER THERAPY

A variety of natural and genetically modified nonpathogenic bacterial species are being explored as potential antitumor agents. The use of bacterial toxins is another aspect of the application of microorganisms to cancer therapy.¹¹⁹ One example of a clinical trial involving the use of bacteria is the use of VNP20009, a genetically modified strain of *Salmonella typhimurium*, for advanced or metastatic solid tumors. Furthermore, intravesical bacillus Calmette–Guérin (BCG), an attenuated mycobacterium developed from the *Mycobacterium bovis* strain used for tuberculosis vaccination, has become the treatment of choice for high-risk superficial bladder cancer in most countries because it provides superior protection from tumor recurrence and even reduction of disease progression.¹²⁰ Patients treated with intravesical BCG plus interferon have a 60–70% chance of a complete and durable cure. Although its precise mechanism of action has not been clearly determined, the intense local immune activation after BCG correlates with pronounced infiltration of the bladder wall by immunocompetent cells together with the secretion of cytokines.

Bacterial toxins have also entered clinical trials as anticancer agents. Examples are Tf-CRM 107 and IL-4–PE (IL-4–*Pseudomonas* exotoxin), a transferrin–diphtheria toxin conjugate assayed for brain tumors, and IL-13–PE –(IL-13–*Pseudomonas* exotoxin), which is under assay for several kinds of tumors.

REFERENCES

- 1 Kohler G, Milstein C. *Nature* 1975;**256**:495.
- 2 Segota E, Bukowski RM. *Cleveland Clin J Med* 2004;**71**:551.
- 3 Weiner LM, Adams GP, von Mehren M. In: DeVita VT, Hellman S, Rosenberg SA, editors. *Cancer: principles & practice of oncology*. 6th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001. p. 495.
- 4 (a) Lim SH, Beers SA, French RR, Johnson PWM, Glennie MJ, Cragg MS. *Haematologica* 2010;**95**:135;
(b) For a review, see Alduaij W, Illidge TM. *Blood* 2011;**117**:2993.