Ambulatory chemotherapy: what community and hospital pharmacists need to know

Racha Sabbagh Dit Hawasli, Pharm.D,
PhD candidate

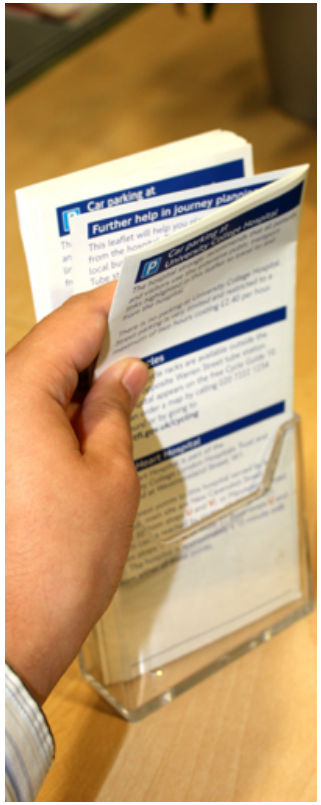
Supervisors:
Shereen Nabhani-Gebara, Pharm.D, BCOP
Stephen Barton, PhD, CSci, CChem, MRSC.
Reem Kayyali, PhD, MSc, BPharm, MRPharmS

Ambulatory Chemotherapy

The provision of chemotherapy infusions to patients on an ambulatory basis using a portable infusion device[1]

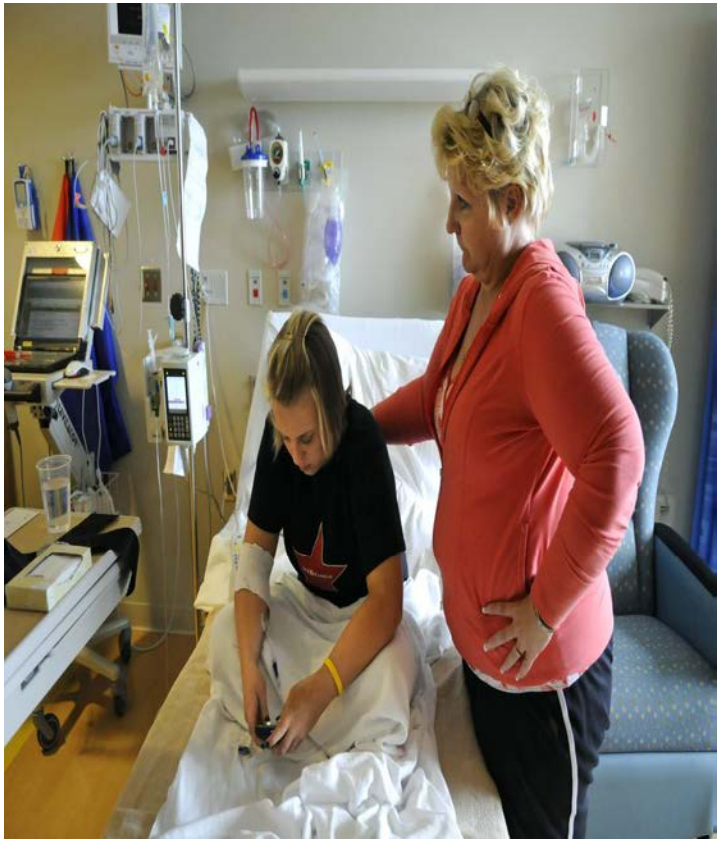
(1) Lee YM, Hung YK, Mo FKF, Ho WM. Comparison between ambulatory infusion mode and inpatient infusion mode from the perspective of quality of life among colorectal cancer patients receiving chemotherapy. *International Journal of Nursing Practice*. 2010;16: 508–516
(2) Preset, 2014, Summit Medical Products Ambit Infusion Pumps, digital photograph, Accessed on 2nd July 2014, http://www.ambitpump.com/ambulatory-infusion-pumps
(3) Ambulatory Infusion Pump, digital photograph, HIWTC, Accessed on 2 July 2014, http://www.hiwtc.com/products/ambulatory-infusion-pump-2836-10816.htm

Ambulatory Chemotherapy



(17) Sophisticated elastomeric technology, 2015, digital photograph, Admedus, Accessed on 17 March 2015, http://uat.admedus.com/au/product/dosi-fuser/
(18) Digital photograph, Patients and Visitors, Patient Information Leaflets, University College London Hospitals NHS, Accessed on 17 March 2015, https://www.uclh.nhs.uk/PandV/PIL/Pages/Home.aspx
(19) Leannology, 2015, digital photograph, Accessed on 20 March 2015, http://www.leannology.com/2012/11/11/the-wheeeeeze/

Ambulatory Chemotherapy



(20) Patient with connected ambulatory pump. Accessed on 30 November 2014, http://2.bp.blogspot.com/-vX5exGBHB3E/TVsh_Pp4drI/AAAAAAAABjg/V8nKx4Bdmtc/s320/pump1.jpg

Patient testimonial

Outline

- Pump design
- Current use
- Use in Lebanon
- The future

Elastomeric Infusion Pumps

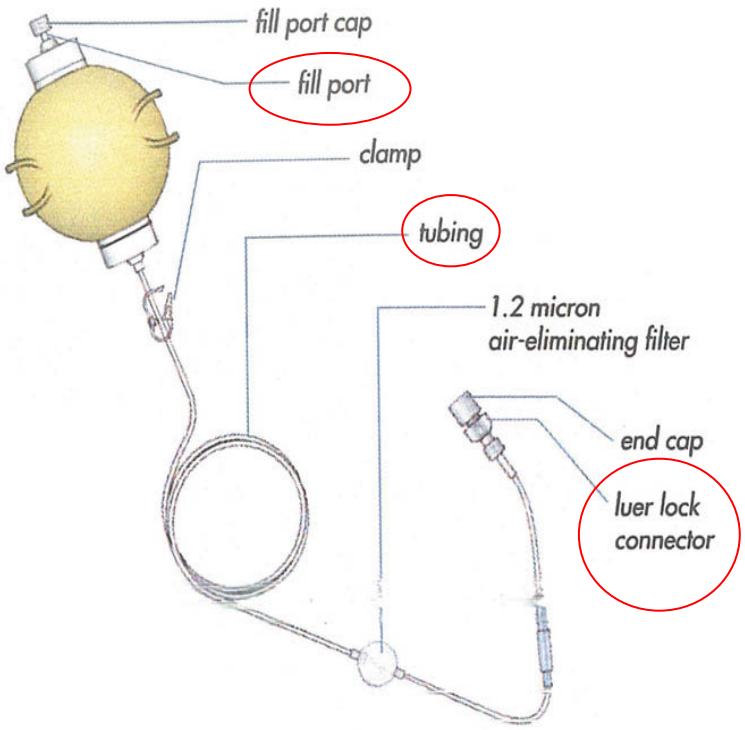
PUMP COMPONENTS

-Outer protective shell
- Inner elastomeric “balloon” continuously deflating and driving the liquid through the IV line

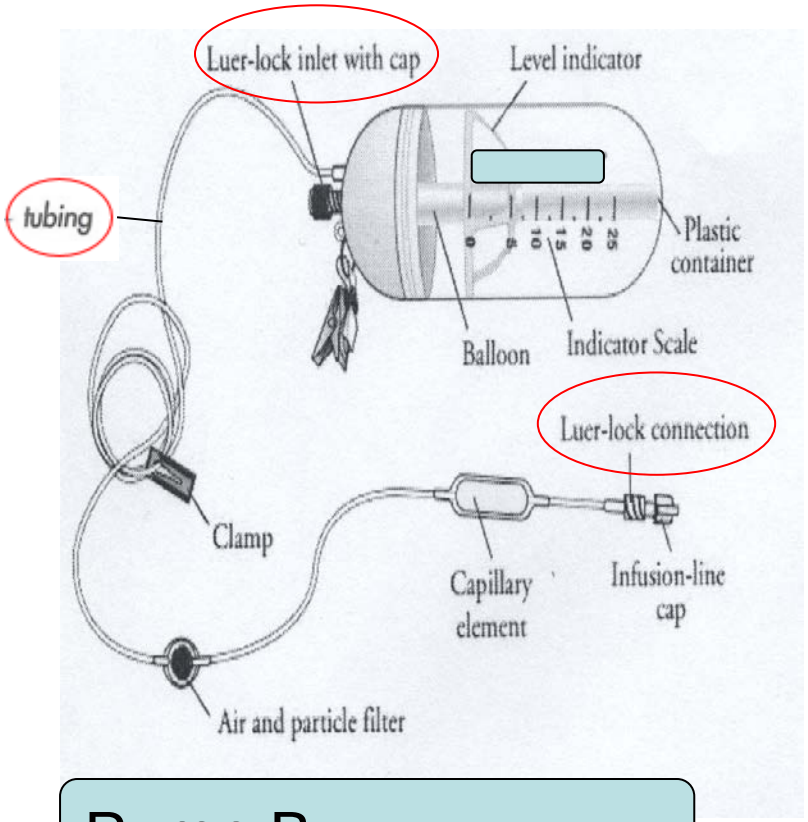
(4) Having chemo by chemotherapy pump, 2015, digital phototgraph, Chemotherapy Pumps, Cancer research UK, Accessed on 2 July 2014, http://www.cancerresearchuk.org/about-cancer/cancers-in-general/treatment/chemotherapy/having/chemotherapy-pumps
(5) *Pressure*, 2014, digital photograph and vector, Summit Medical Products Ambit Infusion Pumps, http://ambitpump.com/pressure-concepts
(6) Baxter Elastomeric Pumps. Clinician Guide”. *Baxter*. Health Technology Safety Research Team. N.d. Web. Retrieved July 1st 2014 from: http://www.capca.ca/wp-content/uploads/Baxter-Elastomeric-Pumps-Clinician-Guide11.pdf

Elastomeric Infusion Pumps

PUMP COMPONENTS



Pump A



Pump B

(7) Elastomeric Pump 100ml Volume 0.5 ml / hr. Vector. Accessed on May 20th 2015. www.shopmedvet.com
(8) Dosi fuser pump. vector. Accessed on May 21st 2015. www.omnimedicalsupply.com

Elastomeric Infusion Pumps

Different capacities and flow rates to suit all regimens

(9) Baxter folfusor 2ml/hr: BAXTER FOLFUSOR SV 2 ML/H 48 HR. Digital photograph. Accessed on May 21st 2015. www.absolutmedicalhealthcare.com
(10) Baxter folfusor 2.5ml/hr: BAXTER FOLFUSOR SV 2,5 ML/H 2 DAYS. Digital photograph. Accessed on May 21st 2015. www.absolutmedicalhealthcare.com
(11) Baxter folfusor 5ml/hr: BAXTER FOLFUSOR SV 5 ML/H 1 DIA. Digital photograph. Accessed on May 21st 2015. www.absolutmedicalhealthcare.com

Elastomeric Infusion Pumps

Applications

- Infusing antibiotic, pain management medication, iron chelation, chemotherapy
- Some chemotherapy protocols provided on ambulatory basis: 5FU, Ifosfamide+Mesna, Trabectidin, etc.

(12) Romain Coriat, Olivier Mir. (2010) Ambulatory administration of 5-day infusion ifosfamide + mesna: a pilot study in sarcoma patients. *Cancer chemotherapy and pharmacology, 65*(3), 491-495.
(13) Michael Rubino, James M. Hoffman .Schöffski P, Cerbone L, Wolter P, De Wever I, Samson I, Dumez H, Clement P, Wildiers H, Stas M. Administration of 24-h intravenous infusions of trabectedin in ambulatory patients with mesenchymal tumors via disposable elastomeric pumps: an effective and patient-friendly palliative treatment option. *Onkologie.* 2012;35(1-2):14-7. doi: 10.1159/000335879. Epub 2012 Jan 20.

Elastomeric Infusion Pumps

Advantages	Disadvantages
No progra	
Portable	ent on
Light weig	
Discreet, Silent operation	
Disposable	
No alarm	

Medscape from WebMD

www.medscape.com

http://www.medscape.com/viewarticle/537694

Disposable Infusion Pumps

Elena A. Skryabina; Teresa S. Dunn
Am J Health-Syst Pharm. 2006;63(13):1260-1268. ©2006 American Society of Health-System Pharmacists
Posted 07/07/2006

(14) Elena A. Skryabina; Teresa S. Dunn. (2006) Disposable Infusion Pumps. *Am J Health-Syst Pharm, 63*(13):1260-1268

Factors affecting infusion rate

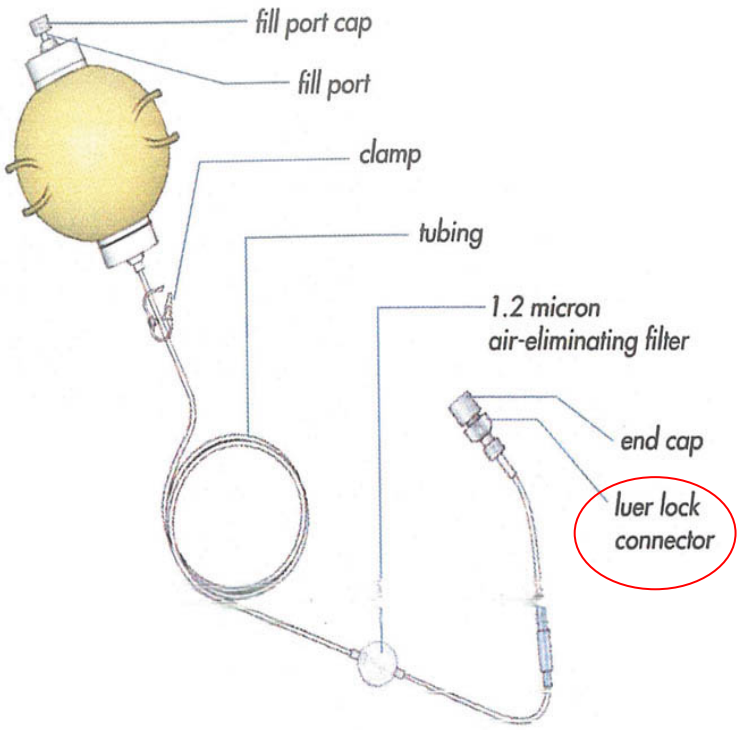
Temperature	~ body temperature	Luer Lock/Capillary element taped to skin
Fill volume	Up to pump Capacity	mL/hr infusion rate
Viscosity of the solution	Dextrose 5% Or 0.9% NaCl	Check manufacturer's guide
Pressure	Ambient	Caution in Hyperbaric/Hypobaric conditions
Pump Height	Luer Lock connector	Caution during sleep and carrying

(6) Baxter Elastomeric Pumps. Clinician Guide". *Baxter*. Health Technology Safety Research Team. N.d. Web. Retrieved July 1st 2014 from: http://www.capca.ca/wp-content/uploads/Baxter-Elastomeric-Pumps-Clinician-Guide11.pdf

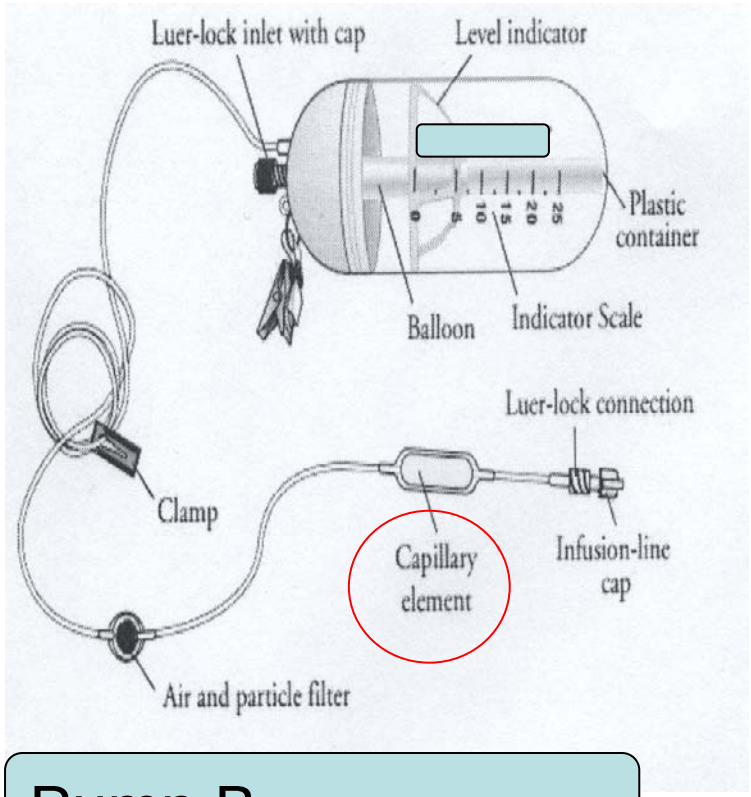
(13) Michael Rubino, James M. Hoffman .Schöffski P, Cerbone L, Wolter P, De Wever I, Samson I, Dumez H, Clement P, Wildiers H, Stas M. Administration of 24-h intravenous infusions of trabectedin in ambulatory patients with mesenchymal tumors via disposable elastomeric pumps: an effective and patient-friendly palliative treatment option. *Onkologie*. 2012;35(1-2):14-7. doi: 10.1159/000335879. Epub 2012 Jan 20.

Elastomeric Infusion Pumps

PUMP COMPONENTS



Pump A



Pump B

(15) Elastomeric Pump 100ml Volume 0.5 ml / hr. Vector. Accessed on May 20th 2015. www.shopmedvet.com
(16) Dosi fuser pump. vector. Accessed on May 21st 2015. www.omnimedicalsupply.com

Factors affecting infusion rate

Temperature	~ body temperature	Luer Lock/Capillary element taped to skin
Fill volume	Up to pump Capacity	mL/hr infusion rate
Viscosity of the solution	Dextrose 5% Or 0.9% NaCl	Check manufacturer's guide
Pressure	Ambient	Caution in Hyperbaric/Hypobaric conditions
Pump Height	Luer Lock connector	Caution during sleep and carrying

Elastomeric-Pumps-Clinician-Guide11.pdf
(13) Michael Rubino, James M. Hoffman .Schöffski P, Cerbone L, Wolter P, De Wever I, Samson I, Dumez H, Clement P, Wildiers H, Stas M. Administration of 24-h intravenous infusions of trabectedin in ambulatory patients with mesenchymal tumors via disposable elastomeric pumps: an effective and patient-friendly palliative treatment option. *Onkologie.* 2012;35(1-2):14-7. doi: 10.1159/000335879. Epub 2012 Jan 20.

Current use

- Used for over 20 years[11]
- Merits:
  - Safe [12, 13]
  - Effective [13]
  - Preferred by patients [1, 13, 14]

(21) Lokich JJ, Perri J, Bothe A., et.al. Cancer chemotherapy via ambulatory infusion pump. *Am J Clin Oncol.* 1983 Jun;6(3):355-63
(22) François Lüthi. Nadia Fucina. Nathalie Divorne. Brigitte Santos-Eggimann. Christine Currat-Zweifel. Patricia Rollier, *et al*.(2012). Home care—a safe and attractive alternative to inpatient administration of intensive chemotherapies. Support Care Cancer; 20:575–581
(23) Michael Rubino, James M. Hoffman et. al. Administration of 24-h intravenous infusions of trabectedin in ambulatory patients with mesenchymal tumors via disposable elastomeric pumps: an effective and patient-friendly palliative treatment option. *Onkologie.* 2012;35(1-2):14-7. doi: 10.1159/000335879. Epub 2012 Jan 20.
(24) Joo EH, Rha SY, Ahn JB, et al. Economic and patient-reported outcomes of outpatient home-based versus inpatient hospital based chemotherapy for patients with colorectal cancer. Support Care Cancer (2011) 19:971–978

Impact

AMBULATORY CHEMOTHERAPY

- Prevents hospital admission
- Waives cost of hospital stay [13,14]

EFFECT ON PATIENT

- Reduced chance of encountering nosocomial infections[14, 15]
- Improved quality of life [15, 16]

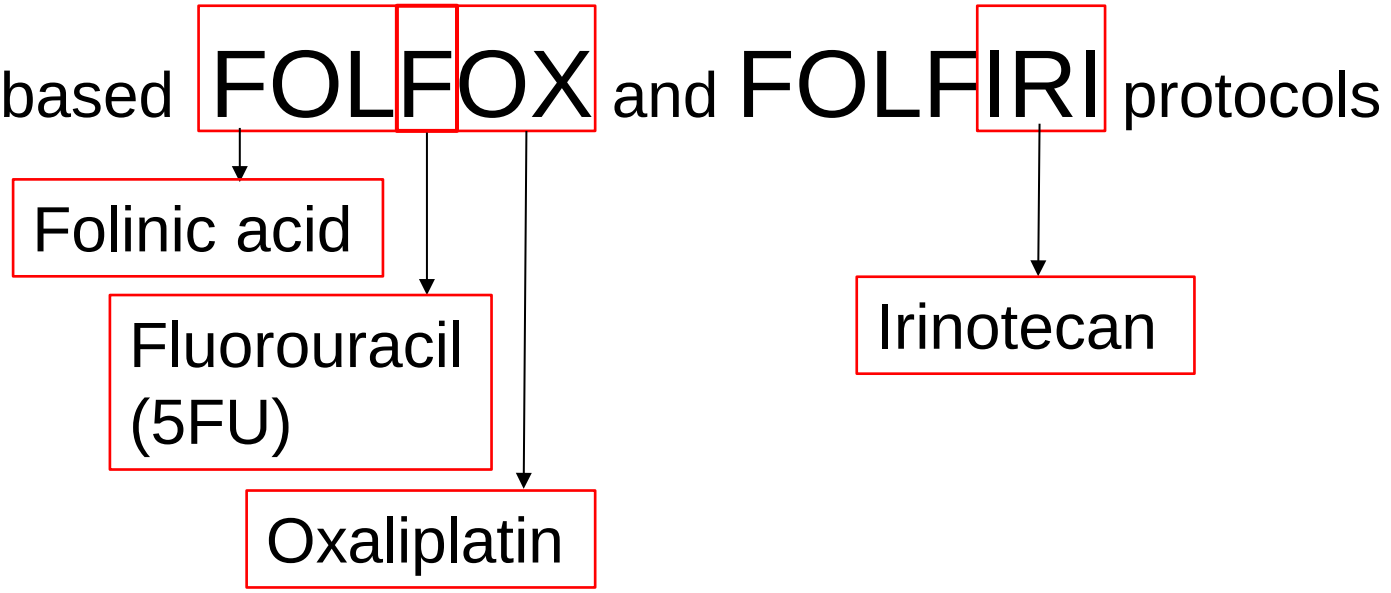
EFFECT ON HOSPITAL

- Reduced bed occupancy [17]
- Reduced hospital work load [1]

(25) Eun-Hye Joo & Sun-Young Rha. Economic and patient-reported outcomes of outpatient home-based versus inpatient hospital-based chemotherapy for patients with colorectal cancer. *Support Care Cancer* (2011) 19:971–978
(26) Hospital Epidemiology and Infection Control in Acute-Care Settings. CLINICAL MICROBIOLOGY REVIEWS, Jan. 2011, WHO [Internet] World health Organization 2002. Prevention of hospital acquired infection. A practical guide, 2nd edition
(27) Michelle Rowe,1 Juan W Valle. New face for a familiar friend: the deGramont regimen in the treatment of metastatic colorectal cancer given as an outpatient: a feasibility study. *J Oncol Pharm Practice* (2002) 8: 97 – 103

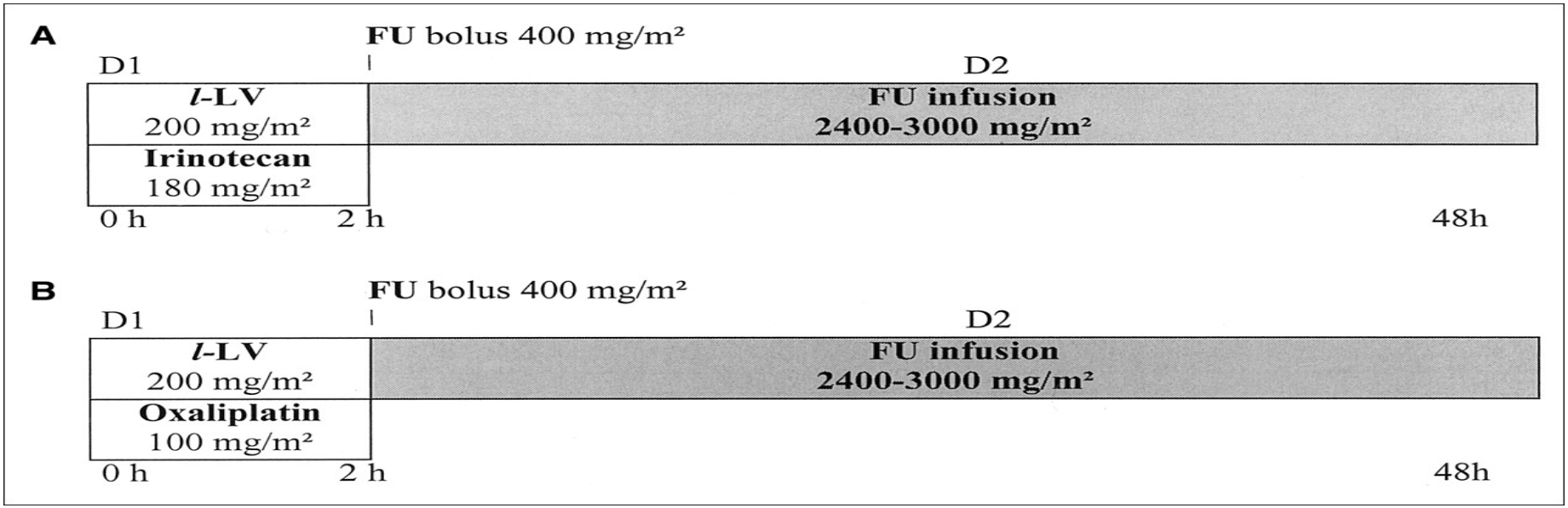
Use in Lebanon

- Use in colon cancer regimens
- Hospital based FOLFOX and FOLFIRI protocols



(28) Marco Tampellini. (2010) Pharmacoeconomic aspects of FOLFIRI or FOLFOX regimens administered with a fully ambulatory pump compared to the day hospital setting. *Tumori*, 96: 438-442

FOLFOX6 FOLFIRI pathway for ambulatory treatment



(A)Simplified leucovorin (*l* -LV) and fluorouracil (FU) every 2 weeks (LVFU2) plus irinotecan (FOLFIRI)
(B) simplified LVFU2 plus oxaliplatin (FOLFOX6)

(29) Tournigand, C, Andre. T, Achille E., et. al. FOLFIRI Followed By FOLFOX6 Or The Reverse Sequence In Advanced Colorectal Cancer: A Randomized GERCOR Study. *Journal of Clinical Oncology* 22.2 (2003): 229-237

FOLFOX6 FOLFIRI pathway for ambulatory treatment

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2015
Colon Cancer

NCCN Guidelines Index
Colon Cancer Table of Contents
Discussion

CHEMOTHERAPY FOR ADVANCED OR METASTATIC DISEASE - CHEMOTHERAPY REGIMENS (PAGE 7 of 9)

FOLFIRI[8]
Irinotecan 180 mg/m² IV over 30–90 minutes, day 1
Leucovorin* 400 mg/m² IV infusion to match duration of irinotecan infusion, day 1
5-FU 400 mg/m² IV bolus day 1, then 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46–48 hours)† continuous infusion
Repeat every 2 weeks

FOLFIRI[8] + Bevacizumab[9,¶]
Irinotecan 180 mg/m² IV over 30–90 minutes, day 1
Leucovorin* 400 mg/m² IV infusion to match duration of irinotecan infusion, day 1
5-FU 400 mg/m² IV bolus day 1, then 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46–48 hours)† IV continuous infusion
Bevacizumab 5 mg/kg IV, day 1
Repeat every 2 weeks

FOLFIRI[8] + Cetuximab[10]
Irinotecan 180 mg/m² IV over 30–90 minutes, day 1
Leucovorin* 400 mg/m² IV infusion to match duration of irinotecan infusion, day 1
5-FU 400 mg/m² IV bolus day 1, then 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46–48 hours)† IV continuous infusion
Repeat every 2 weeks
Cetuximab 400 mg/m² IV over 2 hours first infusion, then 250 mg/m² IV over 60 minutes weekly[11]
or Cetuximab 500 mg/m² IV over 2 hours, day 1, every 2 weeks[12]

FOLFIRI[8] + Panitumumab[13]
Irinotecan 180 mg/m² IV over 30–90 minutes, day 1
Leucovorin* 400 mg/m² IV infusion to match duration of irinotecan infusion, day 1
5-FU 400 mg/m² IV bolus day 1, then 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46–48 hours)† IV continuous infusion
Panitumumab 6 mg/kg IV over 60 minutes, day 1
Repeat every 2 weeks

FOLFIRI + ziv-aflibercept[14]
Irinotecan 180 mg/m² IV over 30–90 minutes, day 1
Leucovorin* 400 mg/m² IV infusion to match duration of irinotecan infusion, day 1
5-FU 400 mg/m² IV bolus day 1, then 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46–48 hours)† continuous infusion
Ziv-aflibercept 4 mg/kg IV
Repeat every 2 weeks

Capecitabine[15]
850–1250 mg/m² PO twice daily, days 1–14
Repeat every 3 weeks

Capecitabine[15] + Bevacizumab[7¶]
Capecitabine 850–1250 mg/m² PO twice daily, days 1–14
Bevacizumab 7.5 mg/kg IV, day 1
Repeat every 3 weeks

See References on COL-C 9 of 9

*Leucovorin 400 mg/m² is the equivalent of levoleucovorin 200 mg/m².
†NCCN recommends limiting chemotherapy orders to 24-h units (ie, 1200 mg/m²/day NOT 2400 mg/m² over 48 hours) to minimize medication errors.
¶Bevacizumab may be safely given at a rate of 0.5 mg/kg/minute (5 mg/kg over 10 minutes and 7.5 mg/kg over 15 minutes).

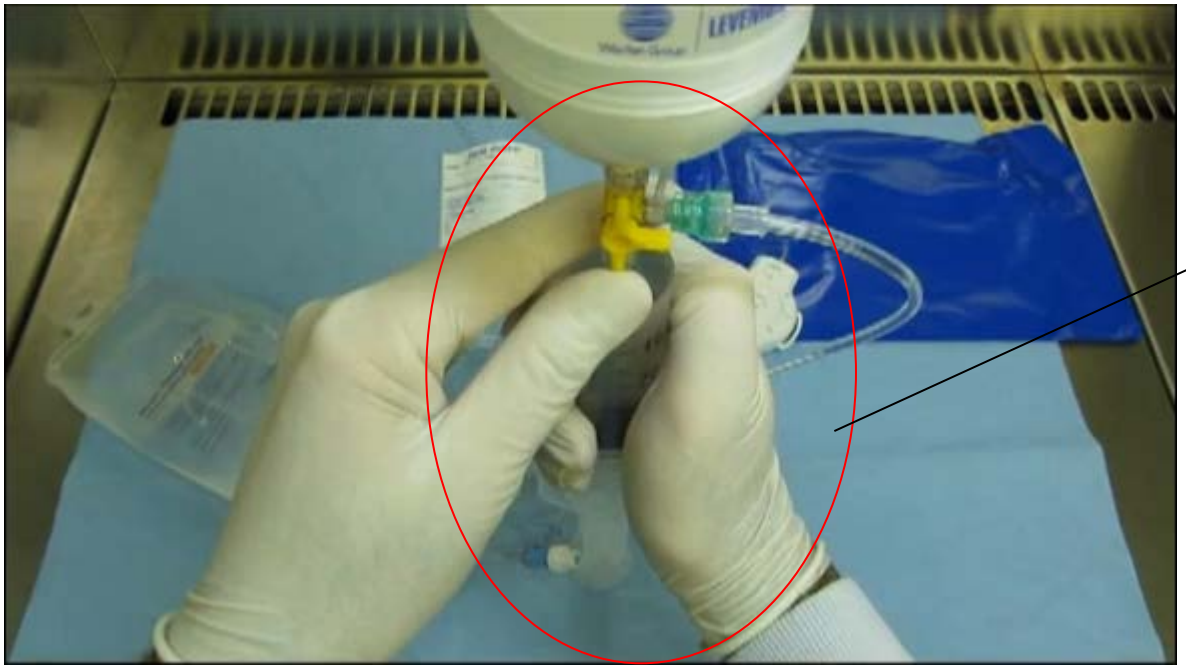
(30) NCCN guidelines: National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology (NCCN Guidelines). Colon cancer. Version 2.2015.[Online]. Accessed on Feb 5th 2015. http://www.tri-kobe.org/nccn/guideline/colorectal/english/colon.pdf

Appropriate pump filling

Needle free

(31) Pump filling. Digital photograph. Accessed on 16th May 2015. https://www.youtube.com/watch?v=b42BpvnSvuo

Appropriate pump filling



Resistance upon filling the pump→ avoid pressure on wrist (Occupational Injury)

(32) Pump filling. Digital photograph. Accessed on 16th May 2015. https://www.youtube.com/watch?v=CB3Mde8iEiI

Patient counselling

Monitor pump emptying depending on flow rate of pump (e.g. 2ml/hr , check 20 mL decrease after 10 hours)

(6) Baxter Elastomeric Pumps. Clinician Guide". *Baxter*. Health Technology Safety Research Team. N.d. Web. Retrieved July 1st 2014 from: http://www.capca.ca/wp-content/uploads/Baxter-Elastomeric-Pumps-Clinician-Guide11.pdf

Patient counselling

- ✓ Cytotoxic drugs used to treat cancer are classified as hazardous
- ✓ Avoid exposing other than patient to contents of pump
- ✓ Carefully clean spill
- ✓ Disconnection at hospital

(33)) NIOSH [2014]. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014. By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP.. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-138 (Supersedes 2012-150)
(34) The Royal Children's hospital Melbourne. Cytotoxic materials are identified by a purple symbol representing a cell in late telophase. Accessed on 17th May 2015. http://www.rch.org.au/rchcpg/hospital_clinical_guideline_index/Cytotoxic_Drugs_The_Management_Of/

Patient counselling

- ✖ Do not submerge pump in water
- ✖ Do not expose to water stream
- ✓ Wrap in plastic bag

- ✓ Keep pump at same height of catheter connection
- ✓ Keep under pillow
- ✖ Do not place above the head

- ✓ Exercise after consulting your healthcare provider
- ✓ Keep pump at room temperature

(6) Baxter Elastomeric Pumps. Clinician Guide". *Baxter*. Health Technology Safety Research Team. N.d. Web. Retrieved July 1st 2014 from: http://www.capca.ca/wp-content/uploads/Baxter-Elastomeric-Pumps-Clinician-Guide11.pdf

The future

In need of *stability data* to move more antineoplastic drugs to ambulatory setting

- Stability profiles extended to days thus saving hospital trips to get the next dose

(35) Salman D, Barton S, Gebara SN. Improving the stability of anticancer drugs. *J Oncol Pharm Pract.* 2014 Jun;20(3):236

The use in Lebanon

Qualitative study performed with stakeholders in Lebanon

- Increase awareness and education to all healthcare professionals
- Patient counselling (leaflets)
- Update the reimbursement schemes to incorporate ambulatory chemotherapy

References

(1) Lee YM, Hung YK, Mo FKF, Ho WM. Comparison between ambulatory infusion mode and inpatient infusion mode from the perspective of quality of life among colorectal cancer patients receiving chemotherapy. *International Journal of Nursing Practice*. 2010;16: 508–516

(2) Preset, 2014, Summit Medical Products Ambit Infusion Pumps, digital photograph, Accessed on 2nd July 2014, http://www.ambitpump.com/ambulatory-infusion-pumps

(3) Ambulatory Infusion Pump, digital photograph, HIWTC, Accessed on 2 July 2014, http://www.hiwtc.com/products/ambulatory-infusion-pump-2836-10816.htm

(4) Having chemo by chemotherapy pump, 2015, digital phototgraph, Chemotherapy Pumps, Cancer research UK, Accessed on 2 July 2014, http://www.cancerresearchuk.org/about-cancer/cancers-in-general/treatment/chemotherapy/having/chemotherapy-pumps

(5) *Pressure*, 2014, digital photograph and vector, Summit Medical Products Ambit Infusion Pumps, http://ambitpump.com/pressure-concepts

(6) Baxter Elastomeric Pumps. Clinician Guide". *Baxter*. Health Technology Safety Research Team. N.d. Web. Retrieved July 1st 2014 from: http://www.capca.ca/wp-content/uploads/Baxter-Elastomeric-Pumps-Clinician-Guide11.pdf

(7) Elastomeric Pump 100ml Volume 0.5 ml / hr. Vector. Accessed on May 20th 2015. www.shopmedvet.com

(8) Dosi fuser pump. vector. Accessed on May 21st 2015. www.omnimedicalsupply.com

(9) Baxter folfusor 2ml/hr: BAXTER FOLFUSOR SV 2 ML/H 48 HR. Digital photograph. Accessed on May 21st 2015. www.absolutmedicalhealthcare.com

(10) Baxter folfusor 2.5ml/hr: BAXTER FOLFUSOR SV 2,5 ML/H 2 DAYS. Digital photograph. Accessed on May 21st 2015. www.absolutmedicalhealthcare.com

(11) Baxter folfusor 5ml/hr: BAXTER FOLFUSOR SV 5 ML/H 1 DIA. Digital photograph. Accessed on May 21st 2015. www.absolutmedicalhealthcare.com

(12) Romain Coriat, Olivier Mir. (2010) Ambulatory administration of 5-day infusion ifosfamide + mesna: a pilot study in sarcoma patients. *Cancer chemotherapy and pharmacology, 65*(3), 491-495.

(13) Michael Rubino, James M. Hoffman .Schöffski P, Cerbone L, Wolter P, De Wever I, Samson I, Dumez H, Clement P, Wildiers H, Stas M. Administration of 24-h intravenous infusions of trabectedin in ambulatory patients with mesenchymal tumors via disposable elastomeric pumps: an effective and patient-friendly palliative treatment option. *Onkologie*. 2012;35(1-2):14-7. doi: 10.1159/000335879. Epub 2012 Jan 20.

References

(14) Elena A. Skryabina; Teresa S. Dunn. (2006) Disposable Infusion Pumps. *Am J Health-Syst Pharm, 63*(13):1260-1268

(15) Elastomeric Pump 100ml Volume 0.5 ml / hr. Vector. Accessed on May 20th 2015. www.shopmedvet.com

(16) Dosi fuser pump. vector. Accessed on May 21st 2015. www.omnimedicalsupply.com

(17) Sophisticated elastomeric technology, 2015, digital photograph, Admedus, Accessed on 17 March 2015, http://uat.admedus.com/au/product/dosi-fuser/

(18) Digital photograph, Patients and Visitors, Patient Information Leaflets, University College London Hospitals NHS, Accessed on (17 March 2015, https://www.uclh.nhs.uk/PandV/PIL/Pages/Home.aspx

(19) Leannology, 2015, digital photograph, Accessed on 20 March 2015, http://www.leannology.com/2012/11/11/the-wheeeeeze/

(20) Patient with connected ambulatory pump. Accessed on 30 November 2014, http://2.bp.blogspot.com/-vX5exGBHB3E/TVsh_Pp4drI/AAAAAAAABjg/V8nKx4Bdmtc/s320/pump1.jpg

(21) Lokich JJ, Perri J, Bothe A., et.al. Cancer chemotherapy via ambulatory infusion pump. *Am J Clin Oncol.* 1983 Jun;6(3):355-63

(22) François Lüthi. Nadia Fucina. Nathalie Divorne. Brigitte Santos-Eggimann. Christine Currat-Zweifel. Patricia Rollier, *et al*.(2012). Home care—a safe and attractive alternative to inpatient administration of intensive chemotherapies. Support Care Cancer; 20:575–581

(23) Michael Rubino, James M. Hoffman et. al. Administration of 24-h intravenous infusions of trabectedin in ambulatory patients with mesenchymal tumors via disposable elastomeric pumps: an effective and patient-friendly palliative treatment option. *Onkologie*. 2012;35(1-2):14-7. doi: 10.1159/000335879. Epub 2012 Jan 20.

(24) Joo EH, Rha SY, Ahn JB, et al. Economic and patient-reported outcomes of outpatient home-based versus inpatient hospital based chemotherapy for patients with colorectal cancer. Support Care Cancer (2011) 19:971–978

(25) Eun-Hye Joo & Sun-Young Rha. Economic and patient-reported outcomes of outpatient home-based versus inpatient hospital-based chemotherapy for patients with colorectal cancer. *Support Care Cancer* (2011) 19:971–978

(26) Hospital Epidemiology and Infection Control in Acute-Care Settings. CLINICAL MICROBIOLOGY REVIEWS, Jan. 2011, WHO [Internet] World health Organization 2002. Prevention of hospital acquired infection. A practical guide, 2nd edition

(27) Michelle Rowe,1 Juan W Valle. New face for a familiar friend: the deGramont regimen in the treatment of metastatic colorectal cancer given as an outpatient: a feasibility study. *J Oncol Pharm Practice* (2002) 8: 97 – 103

(28) Marco Tampellini. (2010) Pharmacoeconomic aspects of FOLFIRI or FOLFOX regimens administered with a fully ambulatory pump compared to the day hospital setting. *Tumori*, 96: 438-442

References

(29) Tournigand, C, Andre. T, Achille E., et. al. FOLFIRI Followed By FOLFOX6 Or The Reverse Sequence In Advanced Colorectal Cancer: A Randomized GERCOR Study. *Journal of Clinical Oncology* 22.2 (2003): 229-237

(30) NCCN guidelines: National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology (NCCN Guidelines). Colon cancer. Version 2.2015.[Online]. Accessed on Feb 5th 2015. http://www.tri-kobe.org/nccn/guideline/colorectal/english/colon.pdf

(31) Pump filling. Digital photograph. Accessed on 16th May 2015. https://www.youtube.com/watch?v=b42BpvnSvuo

(32) Pump filling. Digital photograph. Accessed on 16th May 2015. https://www.youtube.com/watch?v=CB3Mde8iEiI

(33)) NIOSH [2014]. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2014. By Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP.. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-138 (Supersedes 2012-150)

(34) The Royal Children's hospital Melbourne. Cytotoxic materials are identified by a purple symbol representing a cell in late telophase. Accessed on 17th May 2015. http://www.rch.org.au/rchcpg/hospital_clinical_guideline_index/Cytotoxic_Drugs_The_Management_Of/

(35) Salman D, Barton S, Gebara SN. Improving the stability of anticancer drugs. *J Oncol Pharm Pract.* 2014 Jun;20(3):236

Thank you