Dose-banding et préparation à l'avance : Expérience nancéienne

COURS DES - Nancy

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Intérêt de la préparation anticipée pour les hospitalisations de jour

PLAN

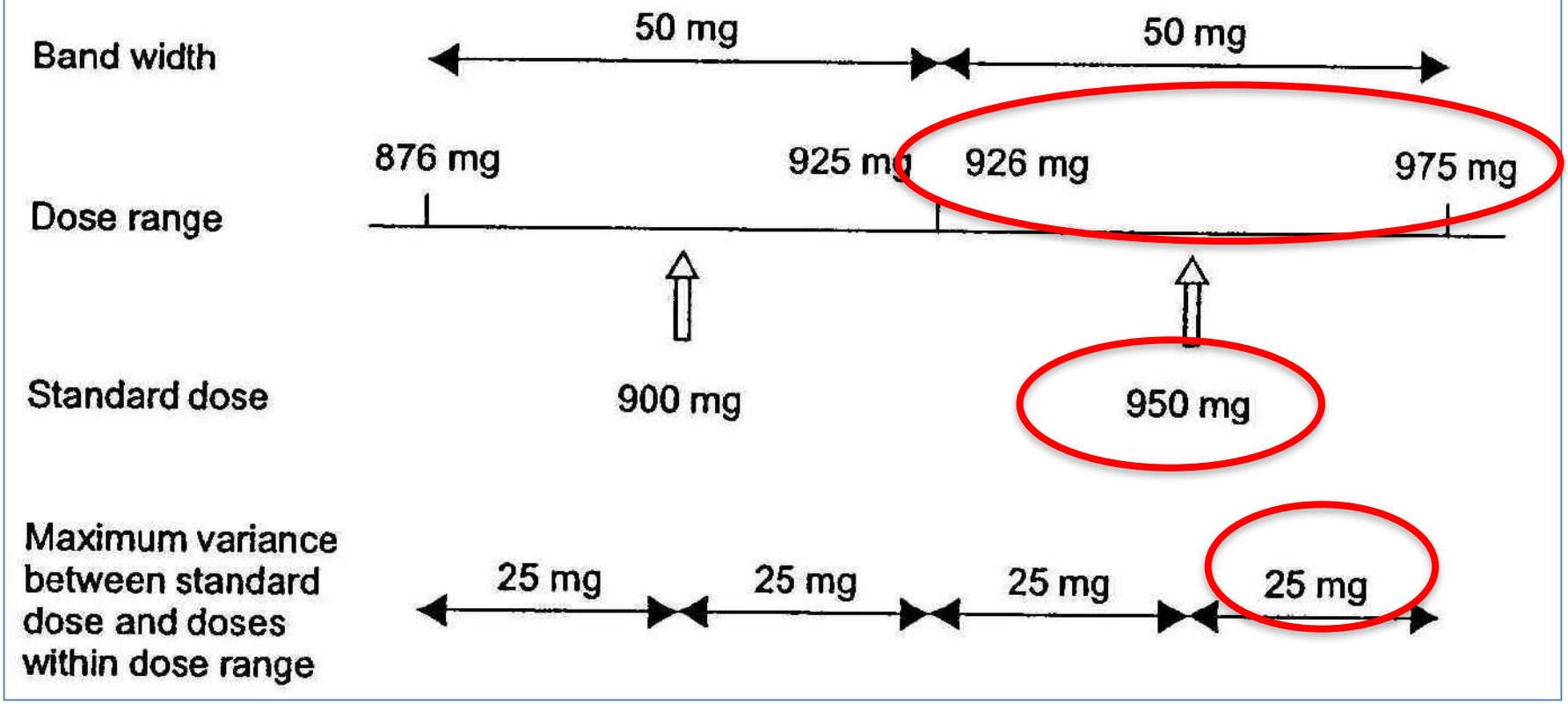
- Introduction
- Le concept de Dose-Banding
- Le Dose-Banding adapté
- Autres types de préparation adaptée

Introduction

- 75% des préparations pour les hospitalisations de jour
  → délais d'attente des patients
  → organisation du service de soin
  → organisation de la production pharmaceutique
  → organisation du contrôle chimique

Le concept de Dose-Banding

Figure 1. Schema of dose-banding with a predetermined band width of 50 mg. In this example, a cytotoxic drug given at 600 mg/m² for a 1.60-m² person (a 960-mg dose) would fall within the dose range from 926 to 975 mg and result in a standard dose of 950 mg being administered.



Ref : Am J Health Syst Pharm 2001; 58: 1760-4

Le concept de Dose-Banding

Table 2.

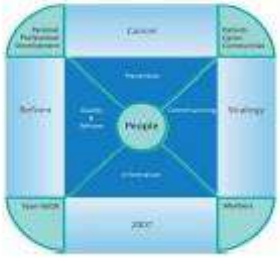
Dose-Banding Scheme for Fluorouracil Based on Grouping by Dose Range[a]

Calculated Dose Range (mg)	Standard Dose (mg)	Syringes Used[b]	Maximum Absolute Variance, mg (%)[c]
776–825	800	400 mg + 400 mg	25 (3.1)
826–875	850	250 mg + 600 mg	25 (2.9)
876–925	900	400 mg + 500 mg	25 (2.8)
926–975	950	250 mg + 300 mg + 400 mg	25 (2.6)
976–1025	1000	500 mg + 500 mg	25 (2.5)

[a]For patients with a body surface area of 1.4–1.7 m^2 receiving fluorouracil 600 mg/m^2.
[b]In this example, prefilled syringes contain fluorouracil 250, 300, 400, 500, or 600 mg.
[c]Absolute difference between the standard dose and the extremes of the dose range. Percentage is based on the difference from the standard dose.

Ref : Am J Health Syst Pharm 2001; 58: 1760-4

Le concept de Dose-Banding



NHS

North of England
Cancer Network

GUIDELINES FOR THE DOSE BANDING OF CANCER CHEMOTHERAPY

"Quality and safety for every patient every time"

Le concept de Dose-Banding

3 Drugs most suitable for dose banding

Not all cytotoxic drugs are suitable for preparation as pre-filled syringes, infusion bags or infuser devices. The key determinant is extended stability, usually an expiry of 30 days or more. Drugs that are currently available with extended expiry include:

- Cyclophosphamide syringes
- Doxorubicin syringes
- Epirubicin syringes
- 5-Fluorouracil syringe
- Methotrexate syringes
- Carboplatin Infusions
- 5-Fluorouracil infusors
- Gemcitabine Infusions
- Oxaliplatin Infusions

These drugs compromise some of the main chemotherapy regimens used in NECN e.g. weekly/ Mayo 5-FU, FOLFOX and FOLFIRI, for colorectal; CMF, FAC, FEC, EC and AC for Breast; CHOP/ RCHOP for lymphoma; CE and Gem Carbo for Lung.

Dose banding has also been applied to other intravenous drugs such as paclitaxel, rituximab and trastuzumab and can also be used for oral preparations e.g. capecitabine.

Le concept de Dose-Banding

5 Suppliers

Some of the main manufacturers of pre-filled syringes for dose banding are listed below. It is noted there are both commercial suppliers and NHS suppliers. Trusts must undertake contracting as described above, however the NECN strategy is to recommend local NHS suppliers.

NHS suppliers

- Newcastle Hospitals NHS Trust Pharmacy
- Leeds Teaching Hospitals
- James Cook University Hospitals

Commercial suppliers

- Baxter Healthcare
- Calea UK Limited
- Dabour Healthcare
- Hospira (formerly Mayne Pharma)
- Qualsept UK

Disclaimer:
This does not represent a comprehensive list of suppliers nor does it in anyway constitute an endorsement of any of the commercial suppliers.

Le Dose-Banding adapté

Exemple du rituximab : étude de stabilité

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Long-term stability of diluted solutions of the monoclonal antibody rituximab

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ABSTRACT

As it is an important challenge for pharmacists to access the stability of monoclonal antibodies because of the widespread of centralized preparation units, we conducted a study to evaluate the physicochemical and biological stability of diluted rituximab at 1 mg/mL over six months at 4 °C. We also conducted the study at 40 °C to demonstrate that all methods employed were stability indicating. Various protein characterization methods were used to determine changes in physicochemical properties of rituximab, including size-exclusion chromatography, dynamic light scattering, turbidimetry, cation-exchange chromatography, second-derivative ultraviolet and infrared spectroscopy, and peptide mapping. Cell culture was used to assess biological stability. We demonstrated that diluted rituximab stored at 4 °C in polyole-

Le Dose-Banding adapté

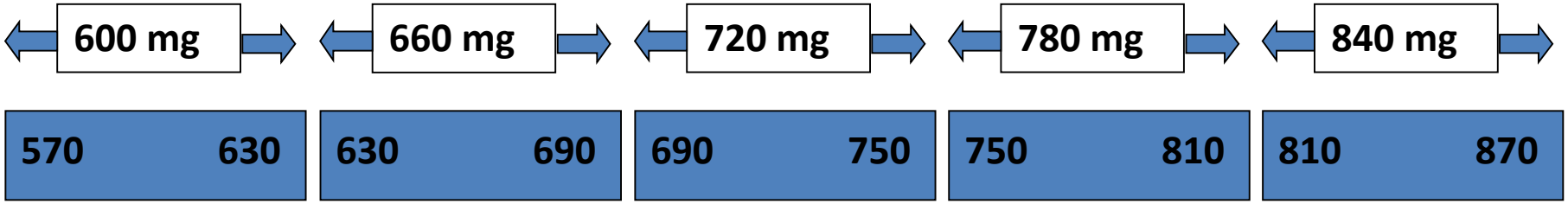
Exemple du rituximab : application en préparation en série

- CHU Créteil Henri Mondor
- Standardisation des doses : 600, 700 mg
- Production en série
- Dispensation au service sans attente

Le Dose-Banding adapté

Exemple du rituximab : application en préparation nominative

- Standardisation par plages de 60 mg entre 570 et 870 mg



- Ecart maximum / dose théorique : 5%
- Préparation à l'avance
- Si annulation, réattribution de la poche selon procédure de réétiquetage sécurisée

Le Dose-Banding adapté

ISOPP Standard

20.4 Procedure for re-use of drugs

20.4.1 Responsible parties

The pharmacy department is responsible for the management of all unused medications returned that were compounded and/or dispensed for oncology patients.

20.4.2 Documentation – medication return(s)

Written policies and procedures about the process/ method of medication return to the pharmacy should be developed and implemented.

Le Dose-Banding adapté

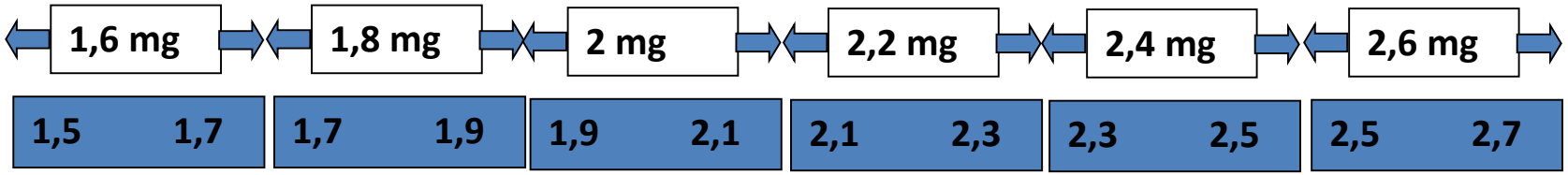
Exemple du bortézomib

- Indication : myélome
- En association avec thalidomide, lenalidomide, dexaméthasone …
- J1, 4, 8, 11
- J1, 8, 15, 22
- Injection
  - IV lente
  - Sous-cutanée
- Donnée labo : stable 8 heures
- Publications : stabilité jusqu'à 35 jours

Le Dose-Banding adapté

Exemple du bortézomib

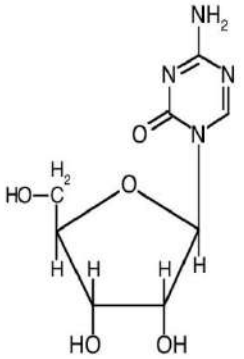
- Standardisation des doses par plages de 0,2 mg entre 1,6 et 2,6 mg



- Ecart maximum / dose théorique : 6,6%
- Préparation à l'avance
- Réattribution de la seringue selon procédure de réétiquetage sécurisée

Le Dose-Banding adapté

Exemple de l'azacitidine

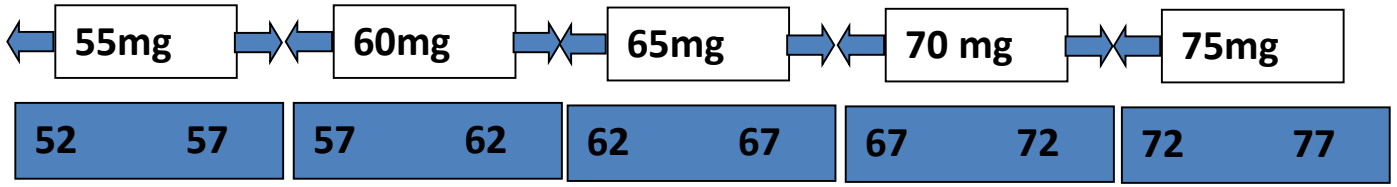


- 75 mg/m² en SC de J1 à J7
- Reconstitution
  - 100 mg avec 4 mL d'eau PPI
  - Suspension à 25 mg/mL d'azacitidine
- Données de stabilité
  - 45 minutes à température ambiante
  - 8 heures au réfrigérateur si eau ppi à température ambiante
  - 22 heures au réfrigérateur si eau ppi réfrigérée (09/2011)
  - **Congelé à -20°C : 1 mois**

Le Dose-Banding adapté

Exemple de l'azacitidine

- Standardisation des doses par plages de 5 mg entre 55 et 75 mg



- Ecart maximum / dose théorique : 5%
- Particularité : destruction si annulation après décongélation

Le Dose-Banding adapté

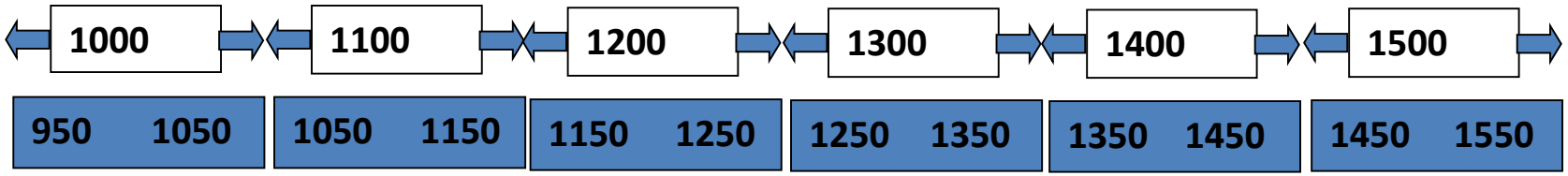
Exemple de la vincristine :

- Deux doses standard 1 et **2 mg**
- Stabilité à 84 jours
  - Trittler R, Sewell G.
  - Stability of vincristine (TEVA) in original vials after re-use in dilute infusions in polyolefin bags and in polypropylene syringes.
  - EJOP 2011; 5,1: 10-14.

Le Dose-Banding adapté

Exemple du cyclophosphamide:

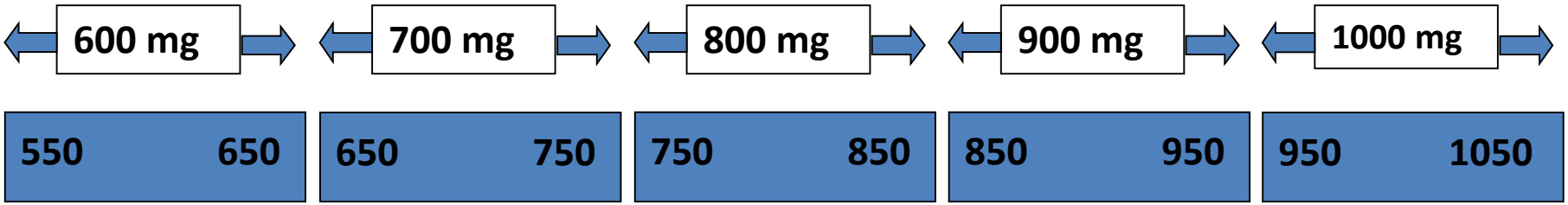
- Standardisation des doses par plages de 100 mg entre 950 et 1550 mg



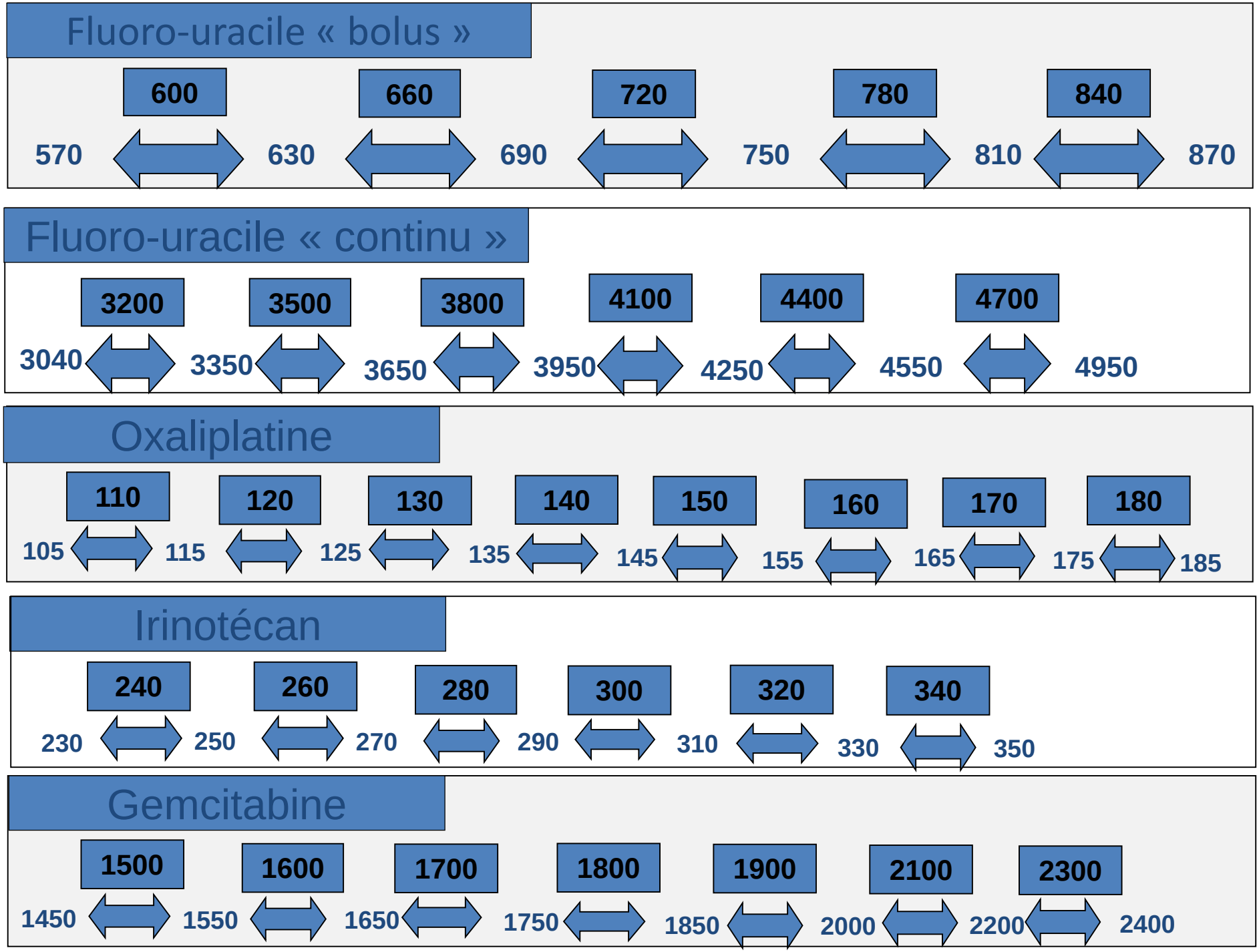
- Ecart maximum / dose théorique : 5%
- Utilisation mixte sur R-CHOP et Neurologie

Le Dose-Banding adapté

Exemple du bévacizumab



- Ecart maximum / dose théorique : 9%
- Neurologie


Fluoro-uracile « bolus »
600
660
720
780
840
570
630
690
750
810
870
Fluoro-uracile « continu »
3200
3500
3800
4100
4400
4700
3040
3350
3650
3950
4250
4550
4950
Oxaliplatine
110
120
130
140
150
160
170
180
105
115
125
135
145
155
165
175
185
Irinotécan
240
260
280
300
320
340
230
250
270
290
310
330
350
Gemcitabine
1500
1600
1700
1800
1900
2100
2300
1450
1550
1650
1750
1850
2000
2200
2400

Interest of dose banding in the preparation of 5-FU infusors in ambulatory care

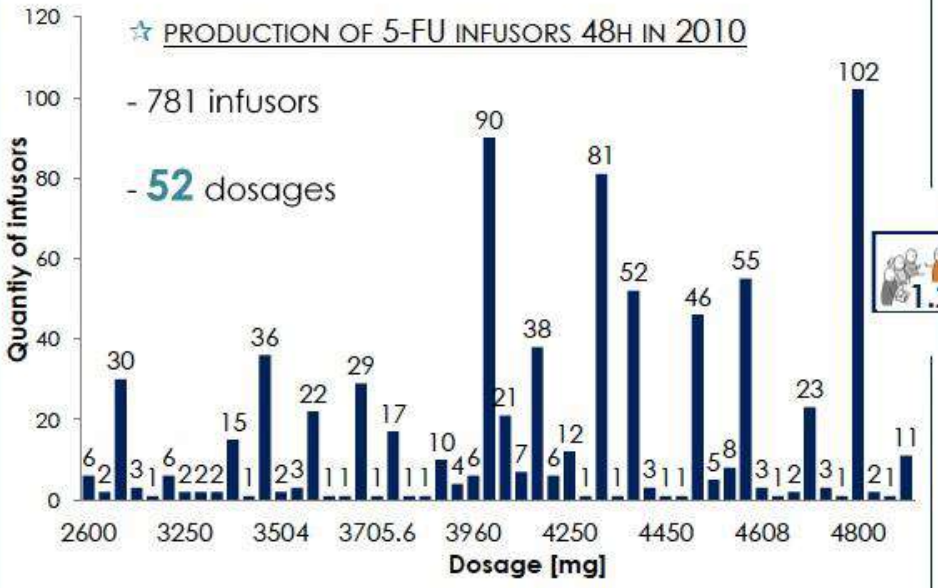
S Martignoni[1,2], G Podilsky[1], B Gay[3], A Pannatier[1,2]

[1]Service of Pharmacy, [2]Multidisciplinary Oncology Center, University Hospital Lausanne, Switzerland, [3]School of Pharmaceutical Sciences, University of Geneva and University of Lausanne, Geneva, Switzerland

4. Results

In 2010, 837 5-FU infusors were produced for **132** patients including **91** different dosages. These infusors included 781 48-hour infusors (93 %), 36 5.5-day infusors and 20 7-day infusors. THE RETROSPECTIVE ANALYSIS home in only on 48-hour infusors .

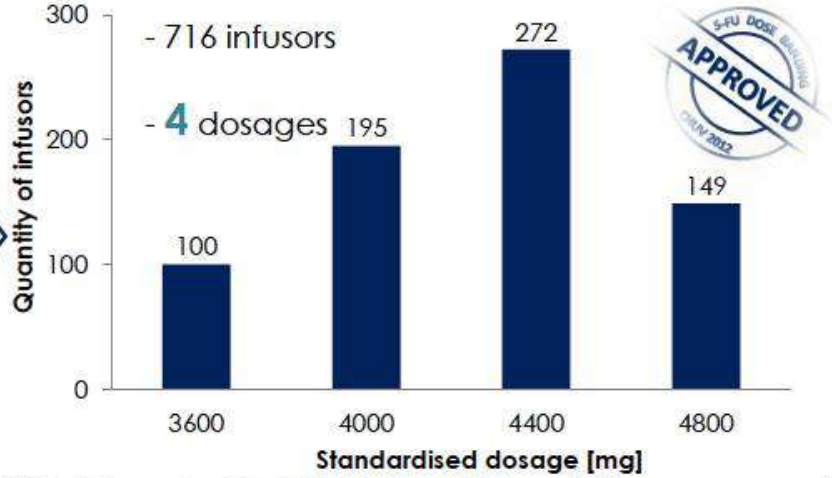
1.1 Retrospective analysis



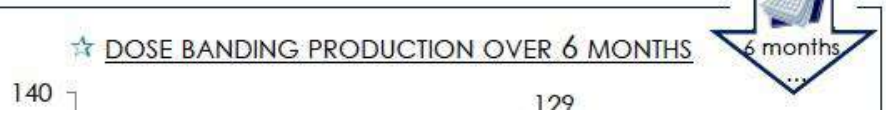
☆ EXPIRED UNADMINISTRATED INFUSORS IN 2011

33 expired infusors (n=932, 3.5 %) were destroyed.

1.3 Selection of standardised dosage



☆ With intervals of ± 5 %, **4 dosages** would have covered **92 %** of preparations



Autres types de préparation adaptée

- Hors HDJ : Toutes les préparations stables des protocoles sur plusieurs jours
  - Cytarabine (sur 4, 5 ou 7 jours)
  - Idarubicine (sur 3 ou 5 jours)
  - Daunorubicine (sur 3 jours)
  - Ifosfamide (IVAM)
  - Cisplatine seringue (R-ESHAP)

Discussion autour de l'anticipation

- Statuts des préparations
  - Préparation magistrale (réalisée extemporanément)
  - Préparation « hospitalière »
    - À l'avance
    - Non nominative
- Pas de statut
  - Préparation à l'avance nominative
  - Réattribution

Discussion autour de l'anticipation

- Indispensable au fonctionnement optimisé des HDJ
  - Temps d'attente des patients diminué ou éliminé
  - Améliore l'organisation de la production
  - Améliore le planning infirmier
  - Permet des économies importantes